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THE HYDROGEN ISOTOPE EFFECT IN THE PYROLYSIS OF ETHYL-1,1,2,2- d_4 ACETATE¹

ARTHUR T. BLADES AND P. W. GILDERSON

ABSTRACT

The hydrogen isotope effect in the pyrolysis of ethyl-1,1,2,2- d_4 acetate has been measured in the temperature range 442–650° C. Making allowance for symmetry numbers in the formation of the ethylene products C_2D_4 and $C_2D_2H_2$, the isotope effect may be expressed as

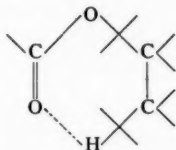
$$k_H/k_D = 0.99e^{11.45/RT}.$$

The data are interpreted as indicating a reaction co-ordinate in which a C—H bond is breaking, but contributions to the isotope effect from residual C—H and (or) incipient O—H vibrations, and from bending vibrations, must be included to explain the results satisfactorily.

INTRODUCTION

Recent studies in the pyrolysis of alkyl esters by Bailey *et al.* (1) as a preparative method for olefins have revived interest in the mechanism of this reaction. Bailey's results were characterized by the almost exclusive production of that olefin which might be described as the least-substituted ethylene, i.e. where competitive reactions were possible, the reaction followed the Hoffmann rule. This selectivity has since been shown (2) not to exist in the homogeneous reaction, the major factor influencing the ratio of products being purely statistical.

The accepted transition state for the reaction is a six-membered ring with the



β -hydrogen of the alkyl group bonded to the acyl oxygen. De Puy and Leary (3) have suggested that the reaction co-ordinate involves the simultaneous breaking of both the C—H and the C—O bonds and the development of double-bond character in the carbon-carbon bond. The alternate possibility of breaking of the C—O bond followed by the C—H bond, which they liken to an E_1 elimination, is ruled out on the basis of relative rates of pyrolysis of substituted benzyl acetates.

More recently, Maccoll (4) has suggested that this reaction may be considered to be "quasi-heterolytic", and likens the elimination to an E_2 type where the rate is primarily determined by the forming O—H bond, rather than by the breaking C—O bond. This

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suggestion has been disputed by De Puy, King, and Froemsdorf (5), who find no evidence of C—O heterolytic bond breaking, and observe a considerable hydrogen isotope effect in the pyrolysis of 1-methyl cyclohexyl-2,2,6,6- d_4 acetate, indicating the importance of the C—H bond breaking in the reaction co-ordinate. Quantitatively, this hydrogen isotope effect, 1.7 at 500° C, and 1.9 at 400° C, is interesting in that it is less than the "theoretical maxima" of 2.1 and 2.3, respectively, which they suggest is due to simultaneous O—H bond formation.

The present study of the intramolecular isotope effect in the pyrolysis of ethyl-1,1,2,2- d_4 acetate allows a more careful appraisal of the effect in a simpler compound.

EXPERIMENTAL

All pyrolyses were carried out in a conventional toluene carrier gas system as has been described previously (6). To extend the temperature range in this pyrolysis, an aluminum furnace with a glass reaction cell of about 10 times the normal volume was used for runs at 443 and 497° C. All runs were carried out at approximately two centimeters of mercury pressure where the ethyl acetate decomposition is known to be first order.

The ethylene products (C_2D_3H and C_2D_4) were separated from the reaction mixture at -80° C, and were freed from traces of toluene and ethyl acetate by passage through a trap at -160° C. The parent peaks in the mass spectrum (masses 31 and 32) were used to determine the ratio of these ethylenes. No allowance was made for sensitivity differences (7), or for possible discrimination in the source of the mass spectrometer, since these would be expected to be small and would affect only the relative frequency factors for the two modes of decomposition.

The ethyl- d_4 acetate was supplied by Merck & Co., and was 99% deuterated as indicated. Since this implies 4% of improperly deuterated ethyl acetate, the assumption was made that this consisted of 2% ethyl-1,1,2- d_3 acetate and 2% ethyl-1,2,2- d_3 acetate; a correction was applied for the production of C_2D_3H from these two impurities.

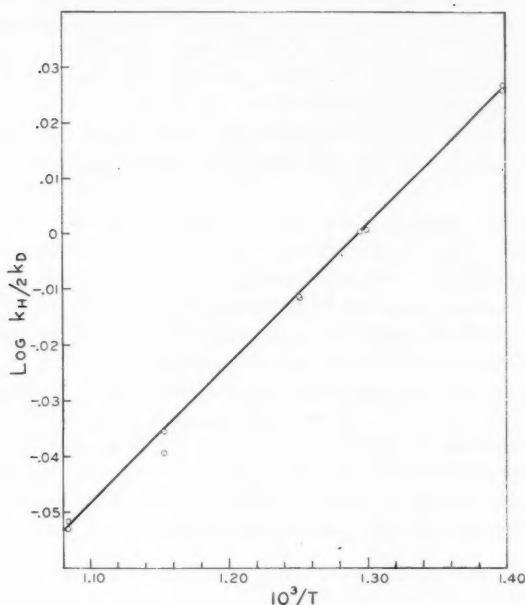
RESULTS

The relative rate data for the production of C_2D_4 and C_2D_3H are presented in Table I, and an Arrhenius plot of the data is shown in Fig. 1. The relative rate constant expression, omitting experiment 2, is

$$k_H/k_D = 0.99 e^{1145 \pm 15/RT}$$

TABLE I
Relative rate data for ethyl-1,1,2,2- d_4 acetate

Expt. No.	Temp., °K	Conversion, %	$C_2D_4:C_2D_3H$	$k_H/2k_D$
1	866.4	50	.891	.922
2	866.7	52	.883	.913
3	922.6	82	.862	.888
4	922.8	90	.860	.886
5	799.4	14	.938	.974
6	799.6	14	.939	.975
7	715.6	11	1.022	1.063
8	715.6	11	1.020	1.061
9	769.2	59	.967	1.002
10	772.2	59	.966	1.001

FIG. 1. Arrhenius plot for the production of C_2D_4 and C_2D_3H .

where allowance has been made for the symmetry number of two in the formation of C_2D_3H , i.e.

$$k_H/k_D = 2 [C_2D_4/C_2D_3H]_{\text{corrected}}.$$

The correction introduced in the activation energy difference by the impurity correction was about 50 cal/mole. In view of the uncertainty in the amount and nature of the impurity, a more realistic uncertainty in the energy term would be ± 50 cal/mole.

DISCUSSION

To interpret the experimental isotope effect in terms of the mechanism of the reaction, the theoretical equation due to Bigeleisen (8) will be used,

$$k_H/k_D = \left(\frac{\mu_D^*}{\mu_H^*} \right)^{1/2} \frac{f}{f^*}.$$

μ_H^* , μ_D^* are the reduced masses in the reaction co-ordinate, and f and f^* are the ratios of the partition functions of the isotopic species for the normal and activated states of the molecule. The function f is defined by the equation

$$f = \frac{s_H}{s_D} \prod_{i=1}^{3n-6} \left(\frac{\nu_D}{\nu_H} \right)_i e^{[h(\nu_H - \nu_D)/2kT]} \left(\frac{1 - e^{-h\nu_H/kT}}{1 - e^{-h\nu_D/kT}} \right)_i,$$

where s_H and s_D are symmetry numbers indicating the number of equivalent atoms

involved in reaction and contribute nothing to the isotope effect,

ν_H and ν_D are the vibrational frequencies of the $3n - 6$ vibrational modes,

h is Planck's constant,

k is Boltzmann's constant, and

T is the absolute temperature.

f^\ddagger is a similar function, the product being taken over the $3n - 7$ vibrational degrees of freedom in the activated complex, excluding the mode associated with the reaction co-ordinate.

For an intramolecular isotope effect, as is being considered here, $f = s_H/s_D$. The isotope effect must then arise in the reduced mass term and in the function f^\ddagger .

It has become conventional to compare experimental hydrogen isotope effects with so-called "maximum" values, obtained by assuming that the only mode making a significant contribution is the stretching mode in the breaking bond, and that residual bonding is lacking in the activated complex. The major contributions to f^\ddagger from C—H and C—D stretching vibrations in the present molecule are from those hydrogens not directly involved in the reaction, i.e. for C—H bond break, there remain two C—D modes, and for C—D bond break, there is one C—D and one C—H mode. The net contribution to f^\ddagger is that from one such vibrational mode; the "Arrhenius" plot for this maximum vibrational contribution, times the reduced mass term (~ 1.4) is shown as curve A in Fig. 2. Curve B is a best fit straight line drawn through curve A over the experimental

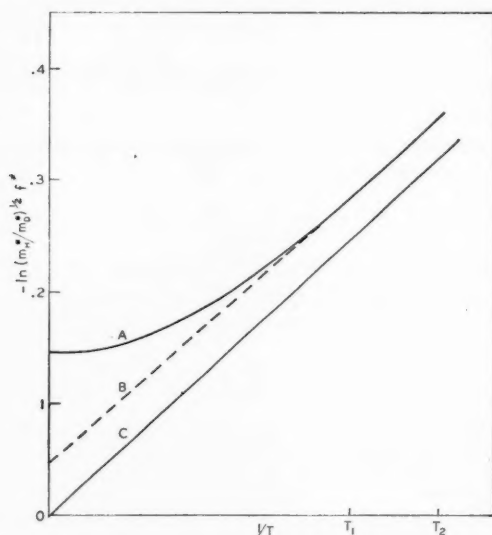


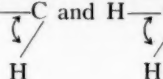
FIG. 2. Arrhenius plots: A, maximum isotope effect from reduced mass term and C—H stretching vibration; B, best fit straight line over the range T_1 to T_2 ; C, experimental plot extrapolated to $1/T = 0$.

temperature range, T_1 (925° K) to T_2 (715° K). This indicates that if just this one mode is contributing to activation, then the experimental isotope effect equation should have a frequency factor ratio greater than one, and an activation energy difference of about 100 cal/mole less than the zero-point energy difference between a C—H and a C—D bond. Curve C shows the experimental equation extrapolated to $1/T = 0$. The lack of

coincidence between curves B and C indicates that this model is not adequate to explain the experimental results.

The contribution to the isotope effect of the function f^* due to residual carbon-hydrogen, or to incipient hydrogen-oxygen bonding, where the reacting hydrogen is considered, is shown in Fig. 3, curves A and B being as previously defined except that the reduced mass ratio is not included. Inclusion of these terms in the isotope effect equation has the effect of further increasing the discrepancy between the model and experiment.

Terms in f^* arising from $\text{C}-\text{C}$ and $\text{H}-\text{C}$ bending modes give rise to the curves



A and A' in Fig. 4, the curve A representing the effect of vibrations of the hydrogen atom involved in the reaction, and the curve A' representing only those hydrogen atoms more or less uninfluenced by the reaction. Since vibrations involving the reacting hydrogen will have the smaller force constants, the total contribution from bending vibrations will be some curve such as A'', and over the experimental temperature range, the Arrhenius line B. Adding these terms to those derived from stretching vibrations will have a tendency to bring the theoretical isotope effect curve more into agreement with the experimental. It must be pointed out that, in view of the appreciable and opposite curvature of the plots in Figs. 3 and 4 in the experimental temperature range, it is necessary to include both of these effects to explain the remarkable linearity of the experimental Arrhenius plot.

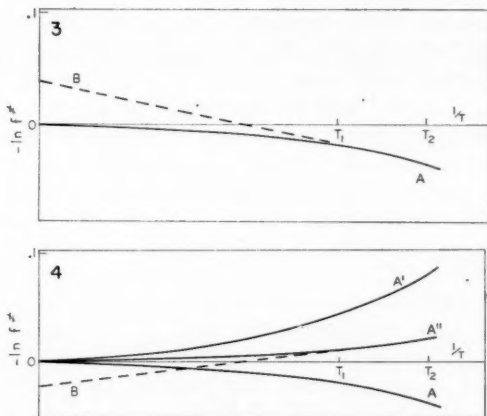


FIG. 3. Arrhenius plots: A, isotope effect from residual C—H stretching; B, best fit straight line over the range T_1 to T_2 .

FIG. 4. Arrhenius plots: A, isotope effect from residual bending, A', from other bending, A'', resultant from all bending; B, best fit straight line over the range T_1 to T_2 .

These isotope effect data are then consistent with a cyclic transition state for the decomposition of alkyl esters, in which the β -hydrogen of the alkyl group is only loosely bound to either the original carbon atom, or the acyl oxygen atom, or both.

This conclusion is in complete accord with the observations of De Puy *et al.* (5) from the decomposition of 1-methyl cyclohexyl-2,2,6,6- d_4 acetate. Their conclusions are based on isotope effects being considerably below "maximum" values, i.e. 2.1 at 500° C and 2.3

at 400° C. Since the present study indicated exactly these values for the isotope effect, it would seem that some appreciable difference in the reaction co-ordinate must exist between cyclohexyl and ethyl esters.

Some support for this view is evident in the pyrolysis of 1-methyl cyclohexyl acetate, where attention is focused on the relative rates of production of the "exo" and "endo" products, methylene cyclohexane and 1-methyl cyclohexene. The expected 60:40 ratio of these products based on the relative number of available hydrogens (which is the major determining factor with straight chain alkyl esters) is quite different from the experimental ratio of 27:73. This, and the low isotope effect, would seem to be consistent with an activated complex for the endo elimination where O—H bond formation is quite important, as suggested by De Puy *et al.*, and where the activation energy would be appreciably lower than for the exo elimination. The invariance of the product ratio over 100° C in this pyrolysis is, however, not compatible with this interpretation.

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The authors wish to thank Drs. M. G. H. Wallbridge and H. W. Habgood for valuable discussions.

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THE SECONDARY HYDROGEN ISOTOPE EFFECTS IN THE PYROLYSIS OF ETHYL- d_5 ACETATE AND ETHYL ACETATE- d_3 ¹

ARTHUR T. BLADES AND P. W. GILDERSON

ABSTRACT

Rate constant expressions have been obtained for ethyl acetate and ethyl- d_5 acetate in the temperature ranges 500–603° C and 501–614° C.

$$k_{\text{(ethyl acetate)}} = 3.86 \times 10^{12} \exp - (48,000 \pm 400/RT) \text{ sec}^{-1}$$

$$k_{\text{(ethyl-}d_5\text{ acetate)}} = 4.84 \times 10^{12} \exp - (49,500 \pm 300/RT) \text{ sec}^{-1}$$

By measuring the relative rate of production of C_2H_4 and C_2D_4 from identical mixtures of the two esters at the temperatures 387 and 490° C, it has been possible to determine the temperature coefficient of the relative rate constant more accurately. This, coupled with the relative rate constants at 500° C derived from the above equations, gives the relative rate constant expression

$$k_H/k_D = 0.8 e^{(115 \pm 25)/RT}.$$

These data are compared with the intramolecular isotope effect in the decomposition of ethyl-1,1,2,2- d_4 acetate, and the differences attributed to secondary isotope effects.

The rate of decomposition of ethyl acetate- d_3 was found to be identical within experimental error with that of the normal acetate.

INTRODUCTION

In the preceding paper (1) it was shown that it was necessary to include bending vibrations and residual and (or) incipient bonding in the activated complex to explain the kinetic isotope effect data on the pyrolysis of ethyl-1,1,2,2- d_4 acetate. In that compound there is relatively little chance for contributions from secondary isotope effects. The comparison of the relative rates of pyrolysis of ethyl and ethyl- d_5 acetates provides an opportunity of evaluating the importance of these effects.

Since this is an intermolecular isotope effect rather than intramolecular as in ethyl-1,1,2,2- d_4 acetate, this pyrolysis serves as a better comparison with the previous isotope effect study on 1-methyl cyclohexyl acetate by De Puy *et al.* (2). This is especially desirable due to their finding of smaller isotope effects than in the d_4 acetate, since in the latter, the occurrence of an isotope effect does not establish that there is an isotope effect in the rate-controlling step.

It has been reported (3) that the pyrolysis of esters of different fatty acids proceed at roughly equivalent rates. It has been found, however, that although ethyl formate and acetate decompose at roughly the same rate, the acetate requires about 4 kcal/mole greater activation energy (4). Believing this to be significant information on the mechanism, an attempt has been made to study the effect of deuteration on the rate of pyrolysis of ethyl acetate- d_3 .

EXPERIMENTAL

All pyrolyses were carried out using the toluene carrier gas technique as has been described previously (5). Since in both rate studies the data had relevance only when compared with normal ethyl acetate, a parallel study was carried out on this compound also. In the ethyl-ethyl- d_5 comparison, alternate runs were carried out under essentially identical conditions with each compound at various temperatures between 500–614° C.

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Experiments were carried out on the ethyl acetate- d_3 at the two extremes of temperature, 502 and 592° C. The percentage decomposition in each case was determined by titration of the acetic acid produced.

Since the isotope effect studies on the ethyl- d_3 acetate gave an unsatisfactorily large error in the activation energy difference, a procedure was developed whereby this could be measured directly, although isotope effects were not measured. The procedure adopted was to mix the ethyl acetate and the ethyl- d_3 acetate as liquids, and then introduce the mixture into the toluene stream for pyrolysis. This provides a mixture of acetates whose composition over a number of experiments, if not constant, is at least changing slowly. This mixture is then decomposed by a small but known amount.

Then, if X_H^0 , X_D^0 are the original number of moles of the normal and deuterated compounds, and k_H and k_D are the corresponding rate constants,

$$\frac{C_2H_4}{C_2D_4} = \frac{X_H^0(1-e^{-k_H t})}{X_D^0(1-e^{-k_D t})} \approx \frac{k_H t X_H^0(1-k_H t/2)}{k_D t X_D^0(1-k_D t/2)}.$$

The approximation is adequate up to about 10% conversion, which must be known to $\pm 0.5\%$, i.e. $10 \pm 0.5\%$; this accuracy is readily achieved.

Since it was unknown how constant the ratio X_H^0/X_D^0 would remain over a series of runs, the system was further complicated by dividing the reactant stream such that one portion was pyrolyzed at high temperature in a small reactor to about 6% conversion, and the other at lower temperature in a 10 times larger reactor to about 1% conversion. Separate product handling systems were provided such that each experiment provided two mixtures of ethylenes.

Then

$$\frac{C_2H_4}{C_2D_4} \bigg|_{T_1} \approx \frac{k_H}{k_D} \bigg|_{T_1} \frac{(1-k_H t/2)_{T_1}}{(1-k_D t/2)_{T_1}},$$

$$\frac{C_2H_4}{C_2D_4} \bigg|_{T_2} \approx \frac{k_H}{k_D} \bigg|_{T_2} \frac{(1-k_H t/2)_{T_2}}{(1-k_D t/2)_{T_2}}$$

which to a sufficient approximation may be written

$$\frac{C_2H_4}{C_2D_4} \bigg|_{T_1} \approx \frac{k_H}{k_D} \bigg|_{T_1} \left[1 - \frac{(\alpha_H - \alpha_D)_{T_1} - (\alpha_H - \alpha_D)_{T_2}}{2} \right],$$

$$\frac{C_2H_4}{C_2D_4} \bigg|_{T_2} \approx \frac{k_H}{k_D} \bigg|_{T_2}$$

where α_H , etc. are the fractional conversions at T_1 , T_2 for the H and D compounds. The temperature coefficient of the isotope effect can then be obtained by an analysis of the two ethylene mixtures and measurements of temperature and approximate conversions in the two furnaces, since

$$\frac{k_H/k_D|_{T_1}}{k_H/k_D|_{T_2}} = e^{\frac{-(E_H - E_D)}{R} \left(\frac{1}{T_1} - \frac{1}{T_2} \right)}$$

where E_H and E_D are the activation energies for the H and D compounds.

The two reactor volumes used were about 30 and 300 cc, the relative contact times being about 1:20. The ethylene ratios were determined mass spectrometrically, masses 27 and 32 being used as representative of C_2H_4 and C_2D_4 respectively. In practice, the C_2D_4 made a small contribution at mass 27; this was subtracted from mass 27 for C_2H_4 estimation. Two sets of analyses were made on each ethylene mixture at fixed sample

pressures as it was found that the ratio of $C_2H_3^+$ to $C_2D_4^+$ varied slightly with sample pressure.

The deuterated ethyl acetates were supplied by Merck & Co., Montreal, and were 99% deuterated as indicated. A correction was applied for 3% of the impurity $CH_3COOCD_2CD_2H$ in the ethyl- d_5 acetate simultaneous pyrolysis experiments. No further purification was attempted on the deuterated compounds.

Rate constant expressions were determined by a least-squares treatment of the rate data, and errors in activation energies were obtained from the average deviation of rate constants from the least-squares line.

RESULTS

The rate data for ethyl and ethyl- d_5 acetates gave the rate constant expressions:

$$k_{(\text{ethyl acetate})} = 3.86 \times 10^{12} \exp(-48,000 \pm 400/RT) \text{ sec}^{-1}, \quad T = 500-603^\circ \text{ C}$$

and

$$k_{(\text{ethyl-}d_5 \text{ acetate})} = 4.84 \times 10^{12} \exp(-49,500 \pm 300/RT) \text{ sec}^{-1}, \quad T = 501-614^\circ \text{ C}$$

the average error in k being $\pm 1.5\%$ and $\pm 1\%$ respectively. A plot of these data is shown in Fig. 1, along with a single rate determination for ethyl-1,1,2,2- d_4 acetate.

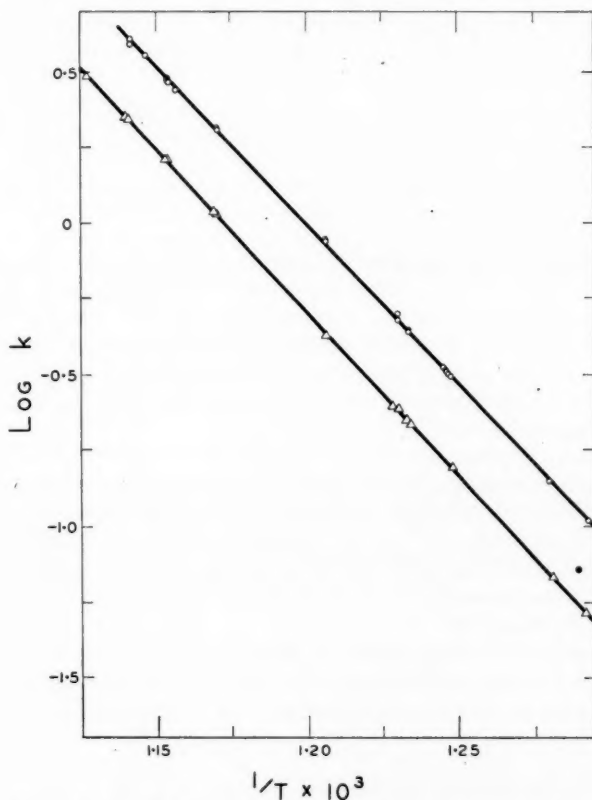


FIG. 1. Arrhenius plot for ethyl, O, ethyl- d_5 , Δ, and ethyl-1,1,2,2- d_4 , ●, acetates.

The results from the direct comparison study are shown in Table I. The average value of " ΔE " is very close to that observed in the separate pyrolysis study, the error being

TABLE I
Data for the copyrolysis of ethyl and ethyl- d_5 acetates
(The duplicate ethylene ratios were determined at different mass spectrometer sample pressures)

Expt. No.	T_1 , °K	T_2 , °K	$C_2H_5^+ : C_2D_5^+$ at T_1	$C_2H_5^+ : C_2D_5^+$ at T_2	ΔE
8	656.8	763.7	2.371	1.971	1590
9	660.5	761.6	2.368 2.300	2.010 1.954	1480 1480
10	661.8	763.6	2.377 2.303	2.007 1.950	1540 1510
11	660.6	763.2	2.377 2.310	2.011 1.961	1490 1460
14	659.9	762.4	2.449 2.381	2.060 2.006	1550 1530
					Av. 1515 \pm 35

reduced from ± 700 to ± 35 cal/mole. The relative rate equation $k_H/k_D = 0.8 e^{1515 \pm 35 / RT}$, $T = 387$ – 490° C, may then be derived, the isotope effect at 500° C being used to fix the pre-exponential factor.

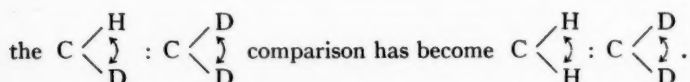
Several rate constant determinations were made on the ethyl acetate- d_3 at 502 and 592° C; no isotope effect in the rate of decomposition could be observed in this temperature range within $\pm 2\%$.

DISCUSSION

In the previous paper on the pyrolysis of ethyl-1,1,2,2- d_4 acetate, the isotope effect was explained on the basis of the reduced mass term and differences in the value of f^* , the value of f being determined solely by symmetry numbers. For the intermolecular isotope effect between ethyl and ethyl- d_5 acetates, the major isotope effect arises in the reduced mass term and f , terms in f^* serving only to reduce the contributions of individual modes of vibration to f . It is therefore convenient to consider only the function f , it being understood that maximum values only are implied.

Since the activated complexes have identical structures in the ethyl- d_4 , and the ethyl and the ethyl- d_5 acetate decompositions, it must be assumed that all of the modes contributing to the primary effect in the former must remain operative in the latter. The major interest in the latter centers then on the decreased frequency factor ratio (0.99 to 0.80) and on the increased activation energy difference (1145 to 1515 cal/mole). All primary effects have been accounted for in the d_4 isotope effect, so these changed constants must be a result of secondary effects.

The most obvious source of these secondary effects is in the bending vibrations at the β -carbon atom, some of which have already been considered in the d_4 compound analysis; the justification for their reconsideration is that their contribution has been increased, e.g.,



An additional, and probably important, source of secondary isotope effects could arise at the α -carbon atom if the C—O bond is breaking in the reaction co-ordinate. Both the

$\text{C} \begin{array}{c} \text{H} \\ \diagup \quad \diagdown \\ \text{O} \end{array}$ bending and further contributions from bending at the β -carbon atom would have

the effect of reducing the frequency factor ratio, and increasing the activation energy difference over the d_4 compound, where these effects could not exist. The coincidence of this model with the observed facts instills considerable confidence not only in the present rationalization, but also in the previous analysis of the ethyl- d_4 acetate data. The suggestion of secondary isotope effects at the α -carbon atom has further interesting implications with respect to the activated complex, suggesting a concerted mechanism, wherein the β -hydrogen transfers to the acyl-oxygen atom simultaneously with the C—O bond break.

A direct comparison can be made between this intermolecular isotope effect and a similar isotope effect in the decomposition of 1-methyl cyclohexyl 2,2,6,6- d_4 acetate (2). For that molecule, De Puy *et al.* found an isotope effect of 1.7 at 500° C and 1.9 at 400° C, whereas in this study our isotope effects at the same two temperatures are 2.1 and 2.4 respectively, slightly higher, in fact, than the intramolecular effect shown by ethyl- d_4 acetate as reported in the previous paper. The inconsistency between the two intermolecular effects supports the view that the reaction co-ordinates of cyclohexyl and ethyl esters are appreciably different.

The failure to observe an isotope effect in the decomposition of ethyl acetate- d_3 lends no support to the suggestion that this methyl influences the rate through an inductive effect. Recently, however, it has been shown by Weston (6) that such an isotope effect, being due to the failure of isotopic molecules to have exactly the same potential energy surfaces, would be immeasurably small for organic reactions. The present results will serve as experimental justification of this theory, if independent evidence for this supposed inductive effect can be found.

ACKNOWLEDGMENTS

The authors are indebted to Dr. M. G. H. Wallbridge and to Dr. R. M. Eloffson for many fruitful discussions.

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KINETICS OF THE THERMAL DECOMPOSITION OF ETHYL PROPIONATE¹

ARTHUR T. BLADES AND P. W. GILDERSON

ABSTRACT

The pyrolysis of ethyl propionate has been studied in the temperature range 505–602° C, yielding the Arrhenius equation

$$k = 5.2 \times 10^{12} \exp(-48,500 \pm 350/RT) \text{ sec}^{-1}.$$

By the copyrolysis of this compound with ethyl-*d*₅ acetate at 384 and 488° C, and comparison of this temperature coefficient with that for the isotopic ethyl acetates, an activation energy difference between ethyl acetate and propionate of 20 ± 65 cal/mole was found, rather than 500 cal/mole as indicated in the individual studies. Since other evidence exists for an inductive effect in the decomposition due to the acid alkyl group, the lack of difference in activation energies is attributed to the change in effect being small and obscured by other effects.

INTRODUCTION

Studies of the kinetics of the pyrolysis of alkyl esters have indicated that the acid group forming the ester has little influence on the rate. Thus Gordon, Price, and Trotman-Dickenson (1), Rudy and Fugassi (2), and Warwick and Fugassi (3) observe about equal rates in the pyrolysis of *t*-butyl formate, acetate, and propionate; similar observations have been made in the pyrolysis of ethyl and isopropyl formates and acetates (4). More recently, Bailey and Hewitt (5) have compared a number of esters of fatty acids, chloroacetic acid, and substituted benzoic acid, and found a correlation of rate with dissociation constant of the acid. Smith and Wetzel (6) have made other correlations, and De Puy, Bishop, and Golders (7) have noted the variability of rate between *sec*-butyl acetate and formate, and monochloro-, dichloro-, and trifluoro-acetate.

Despite the similarity of the rates for formates and acetates, a considerable difference in energy of activation has been observed between ethyl formate (44.1 kcal/mole) (4) and ethyl acetate (48.0 kcal/mole) (8). The view that this difference is the result of the inductive effect of the methyl group on the breaking of the carbon-oxygen bond gains considerable support from the above-mentioned rate data for halo-substituted acetates, where the rate is enhanced by substitution.

The present study of the decomposition of ethyl propionate was undertaken to evaluate the effect of further methyl substitution.

EXPERIMENTAL

The pyrolyses of the ethyl propionate were carried out in a conventional toluene carrier gas system as has been described previously (9), the identical apparatus being used as for the ethyl acetate pyrolysis. Rate constants were determined by titration of the propionic acid produced with 0.1 *N* sodium hydroxide solution.

In the copyrolysis of ethyl propionate and ethyl-*d*₅ acetate, the same technique of pyrolyzing parts of the reaction mixture simultaneously at the two temperature extremes was used as for the ethyl and ethyl-*d*₅ acetates (8), except that the two reactants were introduced into the toluene stream through separate capillaries; hence their proportion was not reproducible for consecutive experiments. The same procedure was adopted for mass spectrometer analysis of the ethylene, and for the correction of the data for isotopic impurities and degree of conversion.

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The ethyl- d_5 acetate (Merck & Co.) was the same sample as used in the previous acetate comparison (8). The ethyl propionate was fractionally distilled and degassed before use.

RESULTS

In the separate pyrolysis of ethyl propionate, variations in contact times from 0.26 to 1.56 sec and pressures from 1.5–2.0 cm Hg showed no effect on rate constants. The Arrhenius rate equation, derived from 15 consecutive runs over the temperature range 505.2–602.4° C is

$$k = 5.2 \times 10^{12} \exp(-48,500 \pm 350/RT) \text{ sec}^{-1},$$

the average error in k being $\pm 1.3\%$. A plot of these data is shown in Fig. 1.

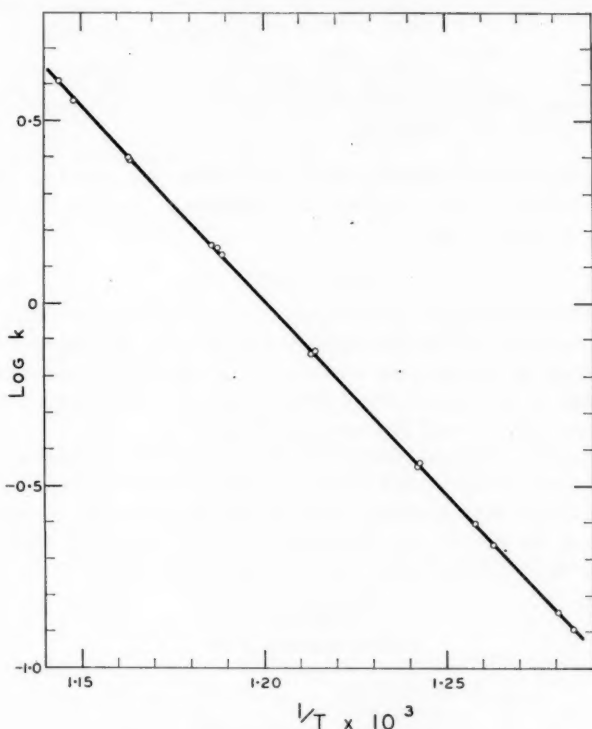


FIG. 1. Arrhenius plot for ethyl propionate.

This Arrhenius equation is to be compared with that for ethyl acetate obtained on the same apparatus,

$$k = 3.86 \times 10^{12} \exp(-48,000 \pm 400/RT) \text{ sec}^{-1}.$$

In the copyrolysis experiments, only four satisfactory experiments were performed; the data for these are presented in Table I. The average value of the difference in activation energy (1495 ± 30 cal/mole) is to be compared with the corresponding value for the

TABLE I
 Relative rate data for ethyl propionate and ethyl- d_5 acetate

Expt. No.	Temperature, °K	Ion ratio, $C_2H_5^+ : C_2D_5^+$	$\Delta \log$ ion ratio (corr.) ^a	ΔE , cal/mole
2	659.4	2.55		
	762.8	2.16	.0671	1490
3	657.0	.218		
	761.1	.184	.0685	1500
4	658.2	.210		
	760.7	.1775	.0693	1550
5	657.8	.328		
	760.7	.280	.0646	1440

^aThis " $\Delta \log$ ion ratio" has been corrected for degree of conversion and for the production of $C_2D_5^+$ from improperly deuterated ethyl- d_5 acetate; it is equivalent to " $\Delta \log k$ " over the temperature range.

ethyl-ethyl- d_5 acetate difference (1515 ± 35 cal/mole) (8). The indicated activation energy difference between ethyl acetate and propionate is then 20 cal/mole within limits of less than ± 100 cal/mole.

DISCUSSION

The purpose of this investigation was to obtain further evidence on a supposed inductive effect of the acid alkyl group on the activation energy for the decomposition of alkyl esters. Although the individual rate constant expression determinations indicated a difference of 500 cal/mole between ethyl propionate and acetate, this was not substantiated by the comparison through the copyrolysis technique.

There is other evidence that an inductive effect is operative in these pyrolyses in that chloro- and fluoro-acetates show much greater rates of decomposition (7) and presumably lower activation energies than acetates. This is in agreement with the opposite electron-sharing character of the methyl and halo-methyl groups as is indicated in the acidity constants of the acids in Table II (10). The relatively large difference in these constants

 TABLE II
 Acidity constants $\times 10^6$

Formic acid	17.7
Acetic acid	1.8
α -Chloroacetic acid	155
Propionic acid	1.3
<i>n</i> -Butyric acid	1.5

between formic and acetic acids dwarfs the difference between acetic and propionic; nevertheless, if a similar effect is operative in the ester decompositions and acid dissociations, the activation energy difference being sought here could have been expected to be several hundred calories.

A possible explanation of the negligible difference found is indicated in the increased acidity constant of *n*-butyric over propionic acid, for which there is no satisfactory

explanation. As suggested by Ingold (10), hyperconjugation may reduce the difference in acidity constants of acetic and propionic acids; such an effect may also be operative in the pyrolyses.

The use of the copyrolysis technique for the determination of differences in activation energy would seem to have wide applicability especially for molecular reactions where there is an interest in a homologous series. The major requirements for reactions to be successfully compared are that they shall proceed at roughly the same rate and that neither products nor reactants shall interfere with the normal course of reaction. A fairly accurate analytical method must be available for one product in each reaction, mass spectrometry seeming to be the most widely applicable, with vapor phase chromatography a possibility.

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THE SYNTHESIS OF HIGHLY RADIOACTIVE ISOPROPYL METHYLPHOSPHONOFUORIDATE (SARIN) CONTAINING P^{32} AS TRACER ELEMENT¹

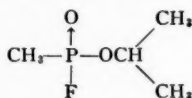
J. B. REESOR, B. J. PERRY, AND E. SHERLOCK²

ABSTRACT

Procedures are described for the safe processing of multicurie quantities of irradiated red phosphorus into isopropyl methylphosphonofluoridate (sarin) having a specific activity of 250 to 300 millicuries per gram. The use of costly remote-handling equipment is avoided by suitable choice of synthetic route and apparatus design.

INTRODUCTION

Several years ago, a requirement arose for radioactively tagged (P^{32}) isopropyl methylphosphonofluoridate (sarin) I, in order to study the biological effects and mode



I

of action of the so-called "nerve gases". The degree of dilution likely to be encountered in such biological studies indicated that quantities of the order of 50 grams with a specific activity of 250–300 mc/g would be required. Safe handling of multicurie sources of radiation is ordinarily achieved by placing operators behind shields and manipulating apparatus with various remote-handling devices. Such devices are complex and costly. Since the hazard depends not only upon the intensity of radiation but the duration of exposure to it, it was visualized that the greater speed of direct handling might give less actual radiation dosage than the much longer exposures to lower levels of radiation attendant on the usual remote-handling operations. The greater surety against accidents provided by direct handling was a further consideration in the synthesis of a highly toxic compound.

Accordingly a careful study of synthetic methods was carried out with a view to elimination of operations requiring long periods of attention. A time study was made of the known alternative routes of synthesis to assess the approximate radiation hazard associated with each procedure. These routes are illustrated diagrammatically in Fig. 1. The results clearly indicated that the route involving the direct conversion of phosphorus trichloride via the APC complex to methylphosphonic dichloride, followed by fluorination to methylphosphonic difluoride and preparation of sarin from the equimolecular mixture of dichloride and difluoride, was the safest practical method to use. The very high yield and purity of the agent produced by this method was a further advantage.

Investigations of this chosen route led to modifications in the chemistry and in the synthetic apparatus used which further simplified the reactions and reduced the hazards considerably. Principally, improvement was obtained in the preparation of methylphosphonic dichloride by an anhydrous procedure (1), which eliminated a filtration, and

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²Present address: Imperial Chemical Industries, Wokingham, Berks, England.

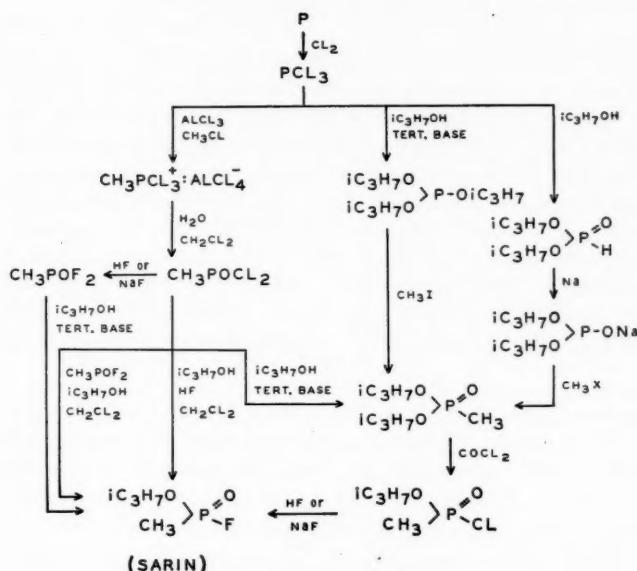


FIG. 1. Synthetic routes to sarin.

the direct conversion of methylphosphonic dichloride to sarin by the use of anhydrous hydrofluoric acid isopropyl alcohol, which eliminated a reaction and a filtration.

Our method is illustrated schematically in Fig. 2.

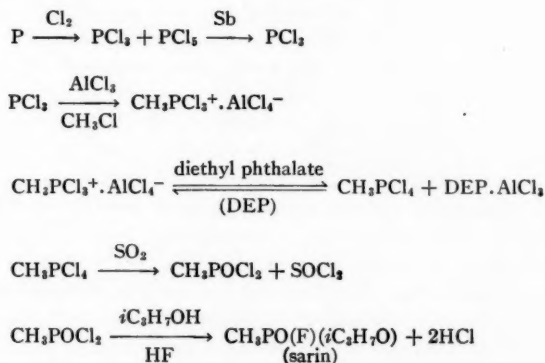


FIG. 2. Chosen synthetic route.

Over a period of approximately 5 years, 12 complete syntheses of sarin (I) containing P^{32} as tracer element have been successfully carried out. The product (I), at the desired specific activity of 250–300 mc/g, was obtained in quantity from 20 to 30 g red phosphorus of specific activity of approximately 2.2 curies/gram.

EXPERIMENTAL

Purification of Red Phosphorus

The phosphorus to be irradiated is purified in our laboratory by treatment of reagent grade material with concentrated hydrochloric acid at reflux temperature for approximately 1 hour, followed by washing with copious quantities of boiling distilled water. Repeated water washing, and decanting from the phosphorus to remove most of the "fines", give a product which is more easily handled since the inclusion of the very fine phosphorus particles sometimes results in a sintered irradiated sample. Finally the phosphorus is filtered, washed with alcohol, ether, and dried in a vacuum desiccator.

When the irradiation was carried out at Idaho Falls, Idaho, the purified red phosphorus was charged into clean, pure (SI grade) aluminum capsules, 15 g of phosphorus per capsule, and sealed in an atmosphere of dry helium. Atomic Energy of Canada at Chalk River do their own packing, and bulk lots of purified phosphorus were sent to them in polyethylene bottles.

Transfer of Irradiated Phosphorus to the Phosphorus Trichloride Apparatus

The transfer of the irradiated phosphorus to the tared PCl_3 reaction flask is accomplished by normal "hot" radiological dry box technique under an atmosphere of dry nitrogen.

Preparation of Phosphorus Trichloride

Phosphorus trichloride is synthesized in the apparatus illustrated in Fig. 3.

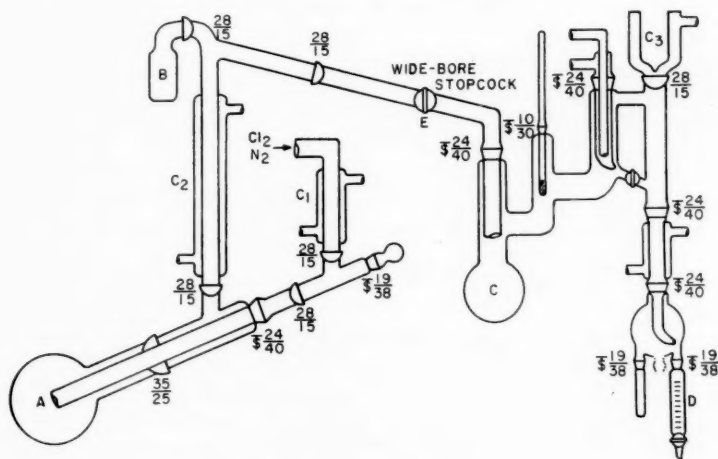


FIG. 3. PCl_3 apparatus.

Approximately 40 grams of dry boiling chips are placed in the reaction flask A, which is then evacuated and heated to dispel as much air as possible from the boiling chips. Dry nitrogen is let into the evacuated flask and the process of heating, evacuation, and admission of dry nitrogen is repeated so as to ensure that all oxygen (which would cause oxidation of the trichloride to oxychloride) is removed. The flask is then stoppered, weighed, and placed in the dry box ready for receipt of the irradiated phosphorus.

The stoppered flask is removed from the dry box after the addition of the irradiated

phosphorus, is weighed to determine weight of phosphorus (approximately 30 grams), and coupled up to the apparatus as shown in Fig. 3.

A slow stream of dry nitrogen is passed into the apparatus through the gas inlet tube to sweep out residual traces of oxygen, and the reaction flask is heated to 110°–120° C. At this stage the slow stream of nitrogen is replaced by a metered stream (6 to 7 liters per hour) of dry chlorine gas and at the same time a jet of cool air is directed on the upper, unheated surface of the reaction flask. Reaction occurs and the phosphorus pentachloride sublimes to the cool upper surface of the flask as it is formed. After 3/4 hour, when a fairly thick crust of phosphorus pentachloride has sublimed to the cool upper surface, chlorination is stopped and a very slow stream of nitrogen (sufficient to maintain a positive pressure only) is substituted for the chlorine. The reaction flask is then rotated through 180° on its ball joint so that the phosphorus pentachloride is covered with unreacted red phosphorus. Heating, without chlorination, is continued for about 15 minutes, by which time the phosphorus pentachloride is largely reduced by the unreacted red phosphorus to phosphorus trichloride. Chlorination is recommenced and the whole procedure repeated until a 20% excess of chlorine has been introduced. Heating is continued for 1 hour or until the residual phosphorus has disappeared.

This stage is fairly easy to observe and is facilitated by the use of boiling chips. Initially glass chips were used to keep the phosphorus mobile, but it was found that they become stained a dark brown by the intense radiation which tends to obscure the end point. The white boiling chips are hardly affected by the radiation and so provide a background against which the unreacted phosphorus is readily discerned.

The mixture in the flask now consists of phosphorus trichloride and phosphorus pentachloride. The mixture is allowed to cool to room temperature. Pure granular antimony (100 g) is then added to the mixture by tipping the antimony container B, which is built onto the apparatus. Powdered antimony reacts very vigorously with phosphorus pentachloride but results in a somewhat inferior product due to the surface film of antimony oxide normally present on the surface of the antimony, giving phosphorus oxychloride as a by-product. Granular antimony reacts more slowly, and a larger excess is required: the product, however, is purer. It is found that -20+80 mesh antimony is most suited to the reaction as a compromise between speed and purity.

Flask C is surrounded by a dry ice - acetone mixture and the nitrogen stream increased to approximately 2 liters per hour to help sweep out the trace amounts of phosphorus pentachloride sublimed into the gas inlet tube and also to prevent phosphorus trichloride distilling too far up the inlet tube in the subsequent operations.

The reaction mixture is then slowly heated. At approximately 75° C a strongly exothermic reaction sets in and phosphorus pentachloride is reduced to phosphorus trichloride by the antimony, antimony trichloride being formed at the same time. When the initial reaction has moderated, it is normal to obtain a yellowish-brown solid precipitate in the reaction mix. Reaction is regarded as complete when the liquid layer in the reaction flask is homogeneous and it has been found that this can only be attained quickly by strongly heating the reaction mixture. The heating mantle temperature is thus slowly raised to 280°–300° C and the elevated temperature is maintained until the liquid layer becomes homogeneous. During this period of heating, the rapidly refluxing phosphorus trichloride washes the last traces of sublimed phosphorus pentachloride into the reaction flask for reduction to trichloride. At the same time some 7–9% of the trichloride, entrained by the slow stream of nitrogen, condenses out in C₃ and is collected in the receiver.

Should there still be yellow solid material in the reaction mix after heating to

280°–300° C for 1 hour, the mixture may be cooled and a further quantity of the antimony added. The initial amount added, however, is a large excess and the further addition of antimony has been required only in those cases where the phosphorus was overchlorinated to give a large quantity of the pentachloride.

When the liquid layer becomes homogeneous the heating mantle temperature is reduced to 230° C, the water removed from the condenser C₂, and the product of phosphorus trichloride distilled in a slow stream of dry nitrogen while maintaining the charge of dry ice – acetone around receiver C. Distillation is continued until white fumes of antimony trichloride are observed in the reaction flask A.

Stopcock E is closed and the crude PCl_3 redistilled from a few grams of antimony to reduce any PCl_5 which might have been sublimed from the reaction flask during the reaction. The receiver is calibrated volumetrically so that the weight of product synthesized may be calculated directly without recourse to weighing and handling the "hot" product.

Yields of pure phosphorus trichloride, based on the phosphorus used, have varied from 92–99%.

Preparation of the Aluminum Chloride:Phosphorus Trichloride:Methyl Chloride (APC) Complex

The apparatus devised for this synthesis is illustrated in Fig. 4. The radioactive phos-

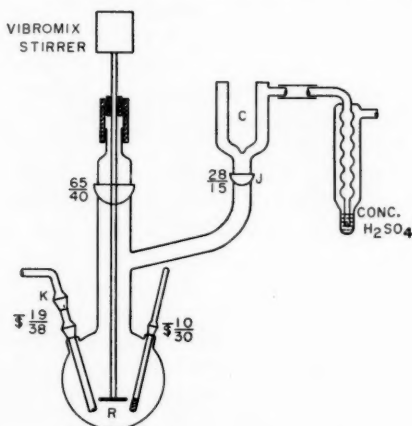


FIG. 4. APC complex apparatus.

phorus trichloride is run into the reaction flask R, which contains 1.5 molar proportions of very finely powdered anhydrous aluminum chloride. The very thick mixture is heated to 70°–75° C and agitated with a "vibrator"-type stirrer of fixed period but variable amplitude. The condenser C is charged with a dry ice – acetone mixture and a slow stream (1 to 1½ liters per hour) of dry methyl chloride is passed into the mixture as close to the point of stirring as possible. In the early stages reaction is slow, but after approximately 1 hour the mixture becomes fluid and the rate of absorption of methyl chloride increases markedly. When the mixture becomes fluid the efficiency of stirring is increased and the rate of addition of methyl chloride stepped up. On an approximate molar scale, absorption of methyl chloride is fairly rapid for approximately 2½ to 3 hours, when the mixture

becomes more viscous and crystals begin to separate on the walls of the flask. At this stage the rate of addition of methyl chloride is reduced to a very slow stream (approximately 1/2 to 1 liter per hour) while heating and stirring are continued. After a further 2 hours the mixture is a semisolid mush of crystals and the reaction is virtually complete. Methyl chloride addition is stopped and heating and stirring are continued for a further hour to ensure completion of the reaction. Heating and stirring are then stopped, the dry ice - acetone is removed from the condenser, and the excess methyl chloride is allowed to boil off. Throughout the whole of the reaction the rate of methyl chloride addition must be carefully controlled so that too great a reflux return to R is not obtained, as otherwise the reaction mixture is cooled below the temperature at which the formation of complex proceeds rapidly. During the period of rapid absorption, the maximum rate of addition of methyl chloride is always used commensurate with maintaining the reaction temperature of 70°-75° C.

Preparation of Methylphosphonic Dichloride from the APC Complex

The apparatus used in the radioactive synthesis is illustrated in Fig. 5.

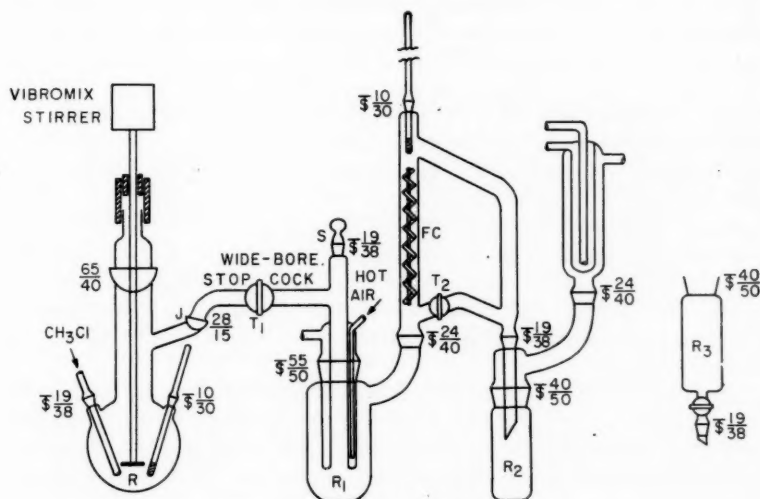


FIG. 5. Methylphosphonodichloride apparatus.

The reaction flask in which the APC complex is prepared is also used for the breakdown of the complex and as the distillation flask for the recovery of the crude methylphosphonic dichloride. On completing the preparation of the APC complex the ball joint J (Fig. 4) is opened and 3 moles/mole complex of dry diethyl phthalate is added to the complex. The joint J is remade and stirring is begun to dissolve the complex as far as possible in the diethyl phthalate. Solution is accompanied by a pronounced rise in temperature and external water cooling should be used to prevent "hot spots" in the early stages until the solid breaks up. At this point a stream (10-12 liters/hour) of dry sulphur dioxide is passed through the stirred mixture via the inlet tube used for methyl chloride. An exothermic reaction occurs and the temperature of the reaction mixture normally rises to a maximum of approximately 50° C, and after approximately 2 hours begins to fall.

Sulphur dioxide is passed into the stirred mixture for a further 30 minutes and the mixture is then allowed to stand for a further 1 hour to ensure completion of reaction. During the passage of the sulphur dioxide the small amount of undissolved but dispersed complex rapidly dissolves and a very fine precipitate of the diethyl phthalate : aluminum chloride complex appears.

On completion of the reaction, the joint J is opened, and the whole reaction flask and contents are transferred to the distillation unit shown in Fig. 5 and joined up via the ball joint J (Fig. 5), the reaction flask then becoming the distillation flask R of Fig. 5. The inlet joint K at the upper end of the gas inlet tube is disconnected and replaced with a capillary air bleed coupled to an air-drying train. The reaction mixture is then thoroughly degassed under water pump vacuum.

The receivers R_1 and R_2 are immersed in dry ice - acetone cooling mixture and the apparatus evacuated by a high-capacity high-vacuum pump to approximately 0.1-0.5 mm Hg. The distillation flask is then heated to 85° to 90° C, when the residual thionyl chloride and methylphosphonic dichloride distill from the diethyl phthalate into receiver R_1 . During the radioactive synthesis 6 hours is allowed, after which time the distillation is considered to be complete. This crude distillation is carried out with the tap T_2 in the open position to avoid a pressure drop which might be caused by the fractionating column FC and to ensure as high a pumping speed as possible at the distillation flask. The taps T_1 and T_2 are then closed, heating is discontinued, the dry ice - acetone cooling mixtures are removed, and dry air is let into the main receiver part of the apparatus.

The receiver R_1 is then heated by a heating mantle and the thionyl chloride is fractionally distilled from the recovered mixture at atmospheric pressure via the column FC. Heating is continued until the temperature at the top of the column is approximately 150°-155° C, which indicated that methylphosphonic dichloride is about to distill. Heating is then stopped and the apparatus allowed to cool to room temperature. The stopper S is replaced by a fine capillary bleed and the receiver R_2 is removed and replaced by the receiver R_3 for methylphosphonic dichloride. The apparatus is evacuated to approximately 60 mm Hg using a water pump and R_1 is again heated to recover pure methylphosphonic dichloride by fractional distillation.

During the evacuation of the apparatus to 60 mm Hg the last traces of thionyl chloride are removed from the upper part of the column and condenser surfaces. At 60 mm Hg the methylphosphonic dichloride distills at 84°-85° C and is distilled at a sufficiently rapid rate to prevent crystallization in the cool parts of the receiver. The product receiver is weighed before and after to determine the yield.

Yields of 88-89%, based on the phosphorus trichloride, are obtained.

Preparation of Radioactive Sarin

The apparatus used in the synthesis is illustrated in Fig. 6.

The dropping funnel which forms the receiver R_3 for the collection of methylphosphonic dichloride in the previous synthesis is transferred to one neck of the three-necked reaction flask and its molten contents are run in. The funnel is washed through into the flask with 100 ml of dry methylene chloride, and the mixture, stirred by means of a magnetic stirrer, is brought to reflux. During this stage of the reaction, water is led through the jacket of the beryl-saddle-packed fractionating column F, so that it acts as a reflux condenser.

A mole/mole solution of anhydrous hydrofluoric acid in anhydrous isopropanol is then prepared. A 5% excess over the theoretical weight of this solution required to react with the methylphosphonic dichloride previously synthesized is introduced into the copper

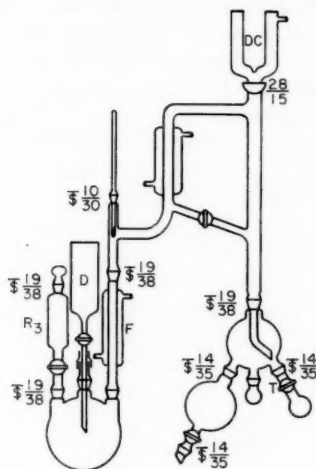


FIG. 6. Sarin apparatus.

dropping funnel D and from there run dropwise into the methylphosphonic dichloride solution at such a rate as to maintain gentle reflux without application of external heat. When addition is complete, the mixture is refluxed for 15 minutes, the water is drained from around the column F, and methylene chloride is distilled off for 15 minutes at atmospheric pressure, by which time evolution of HCl is virtually complete. The remaining methylene chloride is taken off and degassing is completed under water pump vacuum.

At this stage 10 ml of diethylaniline is added, the copper dropping funnel is replaced by a capillary bleed, and fractionation is begun at a pressure of about 10 millimeters. The condenser DC is charged with dry ice - acetone to prevent the loss of sarin which has been found to occur when distilling at this pressure. The forerun is collected in a receiver which may be shut off from the system by means of a tap T when collection is complete, thus preventing its contents from distilling back into the main fraction as distillation proceeds. This measure has been found to increase the purity of the sarin produced from 96-97% up to 99% or better. The main fraction is collected in a dropping-funnel-type receiver to facilitate subsequent dispensing of the product.

Using this method, yields of between 82 and 87% of sarin are obtained. The purity of this material has been found to be consistently better than 99%.

DISCUSSION

Safety

P^{32} is a pure β emitter and these particles are readily stopped by light weight lucite sheets. The bremsstrahlung X rays from such a source as we were handling, however, require thick, heavy metal sheets for complete protection. No laboratory with remote-handling equipment was available at Suffield but after careful consideration of the problem it was decided that the synthetic program could be undertaken using the facilities of our tracer laboratory. The laboratory consists of a main laboratory with seven in-line fumehoods each 5 ft wide and 2 ft 6 in. deep, and auxiliary observation, storage, and changing rooms. The fumehoods are of modern streamline design with all

service outlets inside and to the front whereas all service controls are outside. The hoods can be used singly or jointly as the size of apparatus dictates.

The bases of the fumehoods are of concrete cast in the form of a shallow sink and are lead lined; they are sufficiently robust to allow the heavy screening of local hot spots, such as reaction flasks, with lead bricks or thick sheet lead. The heavy screening of the whole apparatus was found to be impracticable and, in fact, undesirable during general distillation procedures. For general screening work, mobile screens of 1/2-in. thick Lucite (polymethyl methacrylate) faced each side with 1/16-in. steel were found to be ideal. These screens are 15 in. wide and extend the full height of the fumehood face. They run on ball races on permanent tracks along the front of the hoods, and are quickly and very easily moved to the desired screening position. Windows cut in the steel allow observations at the required height and the width of the screen allows an operator to work with his body shielded while using both hands for required manipulations in the fumehood. The steel-lined Lucite screens completely stop all β rays and reduce the bremsstrahlung X rays to approximately 15% of the unscreened value. The main face window of each hood is a vertically rising sheet of 1/2-in. Lucite and is coupled to a damper in the ventilation duct of the hood so that the draft is increased or decreased as the main window is raised or lowered respectively. With the main window completely closed each hood is positively ventilated at a low speed.

The bank of fumehoods is ventilated by a communal system powered by an 8000 cu. ft/min (at 1½ in. static water pressure) exhaust fan. This flow is ample to allow work to proceed safely at three or four fumehoods simultaneously. Inlet air is filtered, thermostatically heated, and enters via the auxiliary rooms into the main laboratory and so to the fumehoods. This system ensures that at all times the operators work in a positive flow of clean air from the clean to the dirty parts of the laboratory.

The concept of dividing the laboratory into "clean" and "dirty" areas was vigorously enforced and easily removed coveralls and boots were worn, as were respirators at all times of transfers in order to eliminate ingestion hazards.

Monitoring of the personnel engaged in the syntheses has been carried out in three ways:

- (i) by plotting the low energy X-ray dosage fields and observing the time spent by each operator at any position,
- (ii) by wearing $\beta\gamma$ film badges, and
- (iii) by wearing pocket dosimeters.

Probably the most important point pertaining to safety is the particular care which must be paid to the design of apparatus and choice of reaction conditions which enable the syntheses to be carried out with a minimum of handling and infrequent observation.

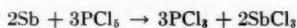
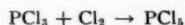
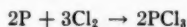
The five-stage synthesis is carried out in 5 days—a total of approximately 60 working hours—by three of the personnel. By dividing the hazardous tasks between the three (monitoring was continuously carried out to facilitate this), each worker receives less than 300 μ r per person, the radiation dosage recommended at that time as the limit for those working continuously with radioactive materials. Since a decay period of at least 3 months is allowed to elapse between syntheses, our experience to date has indicated that complex organic syntheses involving high level sources can be carried out safely without remote handling provided adequate attention is paid to process flow and apparatus design.

Purification of Red Phosphorus

Our first irradiation of commercial red phosphorus graphically illustrated the need for

a preliminary purification of this material. Trace quantities of sodium ion must be eliminated in order to prevent the inclusion of a high-intensity γ source in the starting material.

Preparation of Phosphorus Trichloride



The method (2) of chlorinating red phosphorus to phosphorus trichloride on a large scale, although a straightforward reaction, suffers the disadvantage that an excess of phosphorus must be used to prevent the appearance of the pentachloride in the product. Saunders and Worthy (3) have developed a method for the complete conversion of small (1 g) amounts of phosphorus to the trichloride. Such a method proved impractical on the scale required at Suffield since it required careful standardization of procedures and constant supervision. To avoid waste of the active phosphorus the method of chlorination was modified and advantage was taken of the reducing properties of pure antimony to convert phosphorus pentachloride to the trichloride. The purity of the phosphorus trichloride, checked by infrared spectroscopy, is excellent. The absorption spectrum (Fig. 7) shows a very small percentage of $\text{P}=\text{O}$, much less than by reagent grade commercial product triply distilled in dry nitrogen.

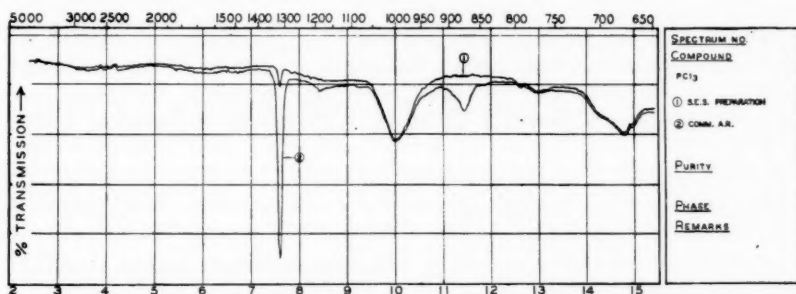


FIG. 7. Spectrum of PCl_3 . (1) Synthetic product; (2) commercial product, AR grade.

Preparation of the Aluminum Chloride:Phosphorus Trichloride:Methyl Chloride (APC) Complex

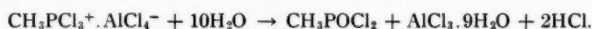
The formation of the 1:1:1 molar aluminum chloride:phosphorus trichloride:methyl chloride (APC) complex proceeds very smoothly in pressure-type apparatus to give yields which are virtually quantitative. When the method is applied to the synthesis of radioactive APC complex, however, it has one marked disadvantage in that the solid has to be transferred from the pressure-type reaction apparatus to the reactor in which the subsequent breakdown of the complex is to be carried out. This introduces a severe radiological hazard since, of necessity, it results in external contamination of the apparatus with consequent risk of ingestion in subsequent operations. The use of the high-boiling electron-donating solvent (used in the breakdown of the APC complex) to dissolve the complex from the pressure reactor reduced, but did not eliminate, this hazard.

Fortunately, it was discovered that the formation of the APC complex at atmospheric pressure proceeds very smoothly at the temperature of refluxing phosphorus trichloride,

and yields are very good provided that loss of the trichloride by the purging action of the methyl chloride passing through the reaction mixture is prevented, and that the reactants are vigorously agitated. The 1:1:1 molar complex can not be made satisfactorily by this method due to the high melting point of this complex, and accordingly an excess of aluminum chloride is used to give a mixture of the 1:1:1 and 2:1:1 aluminum chloride:phosphorus trichloride:methyl chloride complexes, which remain sufficiently fluid for adequate mixing at a temperature of 70°–75° C until absorption of methyl chloride is complete.

Preparation of Methylphosphonic Dichloride

The successful preparation of alkylphosphonic dichlorides was first reported by Kinnear *et al.* (4) and by Clay (5). Their method involved the hydrolysis of a refrigerated solution of the complex in methylene chloride by means of water according to the following reaction:

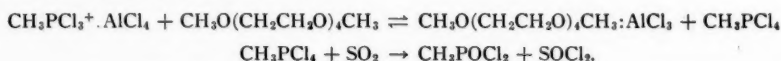


The temperature limits for the hydrolysis (–20° C to –30° C) are critical, and it is essential to filter off immediately the precipitate of the non-anhydrate from this very cold mixture on completion of the reaction. In the laboratory, the high cooling rate could be maintained only by the continuous addition of dry ice. Constant supervision was also required to determine the end point of the hydrolysis.

The breakdown of the complex by this method would prove to be a most difficult and radiologically dangerous part of the synthesis.

An investigation of the breakdown process was made, therefore, and resulted in a novel method, which eliminated almost entirely the excessive hazards intrinsic in the old water hydrolysis reaction scheme. The details of this process, which is completely anhydrous in its function, are reported elsewhere (1). For clarity, however, the following brief account is made.

It was found initially that a high-boiling polyether, dimethoxytetraglycol, not only exhibits excellent solvent properties but also, by complexing with the aluminum chloride itself, frees the phosphorus-containing moiety of the APC complex. The methylphosphonic tetrachloride so liberated reacts smoothly with sulphur dioxide to give thionyl chloride and methylphosphonic dichloride.



The original discovery of the role of dimethoxytetraglycol has been extended to diethyl phthalate, a more stable electron donor.

The methylphosphonic dichloride is readily recovered in excellent yields (80–85% of pure redistilled product) by vacuum distillation.

It can be seen, by comparison with the original aqueous procedure, that the new method has eliminated most of the hazardous procedures; all contaminated residues are left in the flask, no filtration is required, no refrigeration is required, no contaminated volatile gases are evolved, and observation and control are easily effected from a distance.

Preparation of Radioactive Sarin

The two-stage synthesis (reactions 3 and 4) of sarin from methylphosphonic dichloride is relatively simple to carry out and gives good yields of very pure product. The main disadvantage is the radiological hazard which results from the numerous handling

procedures involved in preparing the equimolar di-di (methylphosphonic dichloride and methylphosphonic difluoride) mixture required for the esterification stage.

The mechanism of the di-di reaction (6) clearly indicated that it should be possible to produce sarin from methylphosphonic dichloride by direct esterification and fluorination in one stage provided that the half esterification of the dichloride is carried out in the presence of free hydrofluoric acid. The reaction was investigated using non-radioactive dichloride and was found to proceed smoothly in methylene chloride as a diluent using reaction conditions very similar to those employed in the normal di-di reaction. Distillation of the product from diethylaniline removes last traces of free acid, and the trace amount that codistills with the pure sarin stabilizes the final product. Yields of pure sarin obtained by this method are virtually the same as those by the normal di-di reaction, viz. 82-87%.

The synthesis of sarin by this one-stage process from the dichloride has the following advantages:

(a) The elimination of one stage decreases the time of synthesis and the radiological exposure of the operators.

(b) The handling procedures required in making the equimolar di-di mixture are eliminated.

(c) The over-all yield of sarin from dichloride is increased since the fluorination stage, which gave a 90-92% yield of difluoride, is eliminated as are small losses which were inevitable in making up the accurate equimolar di-di mixture.

The purity of the sarin prepared by the one-stage process, like that of the normal di-di reaction, is better than 99% (7) with careful fractionation.

ACKNOWLEDGMENTS

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ORGANO ARSENIC COMPOUNDS

I. N,N-DIALKYL AMIDODICHLOROARSENITES AND N-ALKYL IMIDOCHLOROARSENITES¹

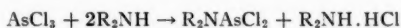
G. A. OLAH AND A. A. OSWALD²

N,N-Dialkyl amidodichloroarsenites were prepared by the reaction of arsenic trichloride with aliphatic secondary amines. Arsenic trichloride and primary amines react similarly, but the N-alkyl amidodichloroarsenites formed usually lose HCl and give N-alkyl imidoarsenites on distillation.

The reaction of aromatic amines with arsenic trichloride has been studied earlier (1-6). These studies were concerned with both the addition reaction and the formation of N-aryl amidohaloarsenites. The main aim of the work reported was to ascertain the mechanism of phenarsazin syntheses.

There are two N,N-dialkyl amidodichloroarsenites described in the literature. In 1896 Michaelis and Luxembourg (7) published the synthesis of "diisobutylamino-dichloro-arsin" by adding diisobutylamine to arsenic trichloride. This method is analogous to that used for the corresponding phosphorus compounds. In 1935 Doak (8) synthesized "diethylamino dichloro arsenamide" by adding arsenic trichloride to a solution of diethylamine in *n*-heptane. When piperidine was used in the place of diethylamine, 20.95% crystalline arsenous acid tripiperidide trihydrochloride and a yellow oil (b.p. 98° C at 1 mm), supposedly piperidinodichloroarsenite, were obtained. No yields were reported for any of these compounds.

In this work the reaction of arsenic trichloride with some aliphatic secondary amines was examined.



By adding 2 moles of secondary amine (dimethylamine, diethylamine, piperidine, morpholine) to every mole of arsenic trichloride (both in benzene solution), the corresponding amidodichloroarsenites were obtained in good yields as is shown in the following table:

TABLE I
N,N'-Dialkyl amidodichloroarsenites
 R_2NAsCl_2

R	R ₂	Boiling point, °C/mm	Refractive index, n_D^{20}	Molecular weight		Chlorine, %		Nitrogen, %		Yield, %
				Calc.	Found (in benzene*)	Calc.	Found	Calc.	Found	
Methyl	Methyl	50-51/10	1.5564	189.9	201	37.34	37.5	7.37	7.41	81
Ethyl	Ethyl	70-71/9†	1.5345	218	235	32.53	32.5	6.42	6.65	78.5
Piperidyl		91/10‡	1.5675	230	248	30.87	31.2	6.09	6.27	75
Morphonyl		125-7/13§	—	231.9	—	30.57	30.8	6.03	6.21	76

* Literature references 12, 14, 15 for method of determination.

† Doak (8) found a boiling point of 107° C at 38 mm.

‡ Doak's compound (8), which boils at 90° C at 1 mm, is different from the piperidinodichloroarsenite obtained by this method.

§ M.p. 87.

|| The compound is only slightly soluble in benzene.

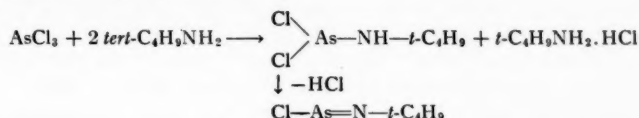
¹ Manuscript received April 19, 1960.

Contribution No. 14 from the Exploratory Research Laboratory of Dow Chemical of Canada, Limited, Sarnia, Ontario.

² Present address: Research Department, Imperial Oil Ltd., Sarnia, Ontario.

The dimethylamido-, diethylamido-, and piperidino-dichloroarsenites are colorless liquids. The morpholidodichloroarsenite is a white, crystalline compound. All of the amidodichloroarsenites which we have prepared are decomposed by water in a violent, exothermic reaction. As a consequence of their sensitivity towards hydrolysis, the liquid compounds "fume" in contact with wet air. They cause an immediate, burning pain and later, blisters appear on contact with the skin.

No literature data were found on the reaction of monoalkyl amines with arsenic trichloride. We have studied the reaction of arsenic trichloride with some simple primary aliphatic amines under the conditions used with the secondary amines. The reaction of *tert*-butyl amine and arsenic trichloride gave a white crystalline compound, also sensitive towards hydrolysis. The analysis of the compound did not correspond to an amidodichloroarsenite, but to an imidochloroarsenite, namely *N-tert*-butyl-imidochloroarsenite. This new type of compound was formed presumably through HCl elimination from the primary amidodichloroarsenite.



Michaelis and Schroeter (10) obtained a phosphorus compound with similar structure (*N*-phenyl imidochlorophosphite) by heating aniline hydrochloride with phosphorus trichloride. They called it benzolphosphazochloride. Arsenimides, which contain an $\text{N}=\text{As}$ (arsazo) bond on the basis of their monomeric structural formula, were obtained by reacting aliphatic or aromatic dichloroarsines with ammonia or primary amines (12, 13). These compounds, like all compounds containing a double-bonded arsenic atom, have multiple molecular weights (12). On the basis of the freezing point depressions of their benzene solutions their molecular weights are 4 times greater than that calculated from the monomeric formula (14). In this work a twofold double molecular weight was found for the *N-t*-butyl imidochloroarsenite, which seems therefore to be present in the dimeric form. The synthesis of *N*-alkyl imidochloroarsenites was also effected with ethylamine and isopropylamine. However, the derivatives obtained in these cases were less stable and they decomposed slightly on vacuum distillation.

TABLE II
Imidochloroarsenites
 $\text{Cl}-\text{As}=\text{N}-\text{R}$

R	Boiling point, °C/mm Hg	Refractive index, n_D^{20}	Molecular weight		Chlorine, %		Nitrogen, %		Yield, %
			Calc. (mono- meric)	Found (in benzene)	Calc.	Found	Calc.	Found	
C_2H_5	155/10 mm dec., m.p. 90–95° C		153.5	505	23.10	25.2	9.12	8.89	71
<i>i</i> - C_3H_7	152–153/10 dec.	1.5964	167.5	527	21.17	21.7	8.36	7.96	65
<i>t</i> - C_4H_9	114–115/10		181.5	375	19.53	19.9	7.72	7.80	66.5

The raw product obtained from the reaction of cyclohexylamine and arsenic trichloride showed good analytical agreement for cyclohexyl amidodichloroarsenite, but decomposed on attempted distillation. The latter fact suggests that the imidochloroarsenites are formed from amidodichloroarsenite intermediates by losing hydrogen chloride.

EXPERIMENTAL

Owing to the sensitivity of the products towards hydrolysis, all the work was carried out with the exclusion of moisture.

N,N-Dialkyl Amidodichloroarsenites

To a benzene solution (200 ml) of 18.1 g (0.1 mole) arsenic trichloride a solution of 0.21 mole aliphatic secondary amine in benzene (50 ml) was added slowly while the mixture was stirred and cooled with ice. Right at the start of the addition the precipitation of amine hydrochloride began. After the addition was completed the mixture was stirred for another 10 minutes and during this time cooling was also maintained to control the exothermic reaction. To complete the reaction cooling was discontinued, but stirring was continued for another half an hour at room temperature. The reaction mixture was then filtered by suction and the precipitate washed with benzene. From the filtrate the solvent was removed by distillation at 100 mm Hg and the raw products were purified by vacuum fractionation at about 10 mm Hg to obtain the corresponding dialkyl amidodichloroarsenites, usually as colorless liquids. Some data on the compounds prepared are shown in Table I.

N-Alkyl Imidochloroarsenites

Arsenic trichloride (18.1 g (0.1 mole)) was reacted with 0.21 mole of the corresponding primary aliphatic amine (ethyl-, *i*-propyl-, *t*-butyl-) as described for the preparation of alkyl amidodichloroarsenites. After the reaction was completed, the solvent was removed by distillation and the remaining raw product was fractionated in vacuum. The alkyl imidochloroarsenites are colorless; if slightly decomposed they are yellow compounds. The *t*-butyl and ethyl compound solidifies after distillation. Yields, physical data, and analytical data are summarized in Table II.

N-Cyclohexyl Amidodichloroarsenites

The reaction between 18.1 g (0.1 mole) arsenic trichloride and 20.9 g (0.21 mole) cyclohexylamine was carried out as described. After volatile components were removed from the filtrate of the reaction mixture at 100° C/10 mm, 17.5 g pale yellow, transparent liquid was obtained. This is a 72.8% yield calculated for *N*-cyclohexyl amidodichloroarsenite. An attempt to distill it at 5 mm resulted in decomposition. $C_6H_{12}NAsCl_2$: molecular weight calculated, 244; found, 508. N%: calculated, 6.71; found, 6.82. Cl%: calculated, 29.06; found, 29.8.

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ORGANO ARSENIC COMPOUNDS

II. N,N-DIALKYL AMIDODIFLUOROARSENITES AND N-ALKYL IMIDODIFLUOROARSENITES¹

GEORGE A. OLAH AND ALEXIS A. OSWALD²

ABSTRACT

The reaction of arsenic fluoride with aliphatic amines was studied. Secondary amines gave N,N-dialkyl amidodifluoroarsenites. Primary amines while reacting similarly lose HF subsequently and yield N-alkyl imidodifluoroarsenites.

The reaction of aliphatic primary and secondary amines with arsenic trichloride was examined in the first part of this work (1). We report now the behavior of these amines towards arsenic trifluoride. On reacting gaseous ammonia and arsenic trifluoride, Besson (2) obtained a solid addition product, $2\text{AsF}_3 \cdot 5\text{NH}_3$. Woolf and Greenwood (3) examined the complex formation of arsenic trifluoride. They found that arsenic trifluoride gives less stable complexes than boron trifluoride or antimony pentafluoride.

By adding 2 moles of a secondary amine to 1 mole of arsenic trichloride in benzene solution, N,N-dimethylamido-, N,N-diethylamido-, and piperidino-difluoroarsenites were synthesized according to the following equation:



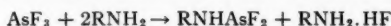
After the amine hydrofluoride was filtered off, the amidodifluoroarsenites were purified by vacuum distillation and obtained as colorless liquids. All these compounds have characteristic odors and are sensitive to hydrolysis.

TABLE I
Amidodifluoroarsenites
 $\text{R}'\text{R}''\text{NAsF}_2$

R'	R''	Boiling point, °C/mm	Refractive index, n_D^{20}	Nitrogen, %		Fluorine, %		Yield, %	Molecular weight	
				Calc.	Found	Calc.	Found		Calc.	Found
Methyl	Methyl	43-44/40	1.4461	8.92	8.89	24.20	24.3	59	157	182
Ethyl	Ethyl	39-40/20	1.4857	7.57	7.59	20.53	20.8	75	185	204
Piperidyl		44-45/10	1.4920	7.10	7.09	19.28	19.5	69	197	206
Cyclohexyl	H	94/9*	—	6.63	6.75	18.00	18.3	67	211	218

*M.p. 65-66.

Some aliphatic primary amines were also reacted with arsenic trifluoride under the same conditions which were used with the secondary amines. Ethyl-, *i*-propyl-, and *t*-butyl-amines gave the corresponding N-alkyl imidodifluoroarsenites.



The latter compounds can be all distilled in vacuum without decomposition. However,

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Contribution No. 15 from the Exploratory Research Laboratory of Dow Chemical of Canada, Limited, Sarnia, Ontario.

²Present address: Research Department, Imperial Oil Ltd., Sarnia, Ontario.

they are sensitive towards hydrolysis. Their molecular weights are 2 to 4 times greater on the basis of the freezing point depressions of benzene solutions than the calculated values for the monomeric formula shown in the above equation. Consequently they are similar to the arsenimides of other type (4) and may be characterized as low molecular weight polymers.

The reaction of arsenic trifluoride with cyclohexylamine under similar conditions did not give N-cyclohexyl imidofluoroarsenite, but instead yielded N-cyclohexyl amidodifluoroarsenite. In this case the primary amine derivative did not lose hydrogen fluoride to form the corresponding imidofluoroarsenite.

TABLE II
Imidofluoroarsenites
(RNAsF)_n

R	Boiling point, °C/mm Hg	Refractive index, n_D^{20}	Nitrogen, %		Fluorine, %		Molecular weight ^a		
			Calc.	Found	Calc.	Found	Yield, %	Calc. (monomeric)	Found
Ethyl	180-182/12	1.5752	10.23	10.61	13.90	13.4	60	137	560
<i>i</i> -Propyl	150-155/9	1.5492	9.27	9.22	12.58	12.6	63	151	775
<i>t</i> -Butyl	91-92/8*	—	8.48	8.52	11.51	11.7	67	175	360

*M.p. 90-91.

EXPERIMENTAL

Arsenic trifluoride was prepared according to Russel, Rundle, and Yost (5), distilled twice, and stored in a polyethylene flask. Absolute benzene and available purest anhydrous amines were used. The work was carried out with the strictest exclusion of air and moisture. The use of arsenic trifluoride (6) and the fluoroarsenite products require careful work since these arsenic compounds have both the properties of arsenic and hydrogen fluoride regarding vapor and contact effect. For molecular weight determination, the freezing point depression of benzene solutions was used.

N,N-Dialkyl Amidodifluoroarsenites

A solution of 0.2 mole of the secondary amine in 50 ml toluene (or benzene) was added slowly to a mixture of 13.2 g (0.1 mole) arsenic trifluoride and 150 ml toluene (or benzene) between 0 and 10° C under cooling and effective stirring. The amine hydrofluoride started to precipitate as soon as the amine addition began. After the addition of the amine was completed, the reaction mixture was kept for an additional 15 minutes below 0° C and then was allowed to come to room temperature. The stirring was continued at room temperature for about 1 hour. Then the amine hydrofluoride was filtered by suction and washed carefully with a small amount of toluene (benzene). From the clear filtrate so obtained the solvent was removed by distillation between 50 and 100 mm. This left the raw products behind as a yellow liquid. It was purified by fractionation in vacuum. In this manner the N,N-dimethylamido-, N,N-diethylamido-, and piperidino-difluoroarsenites were obtained as colorless liquids with an unpleasant smell. Yields, physical data, and analytical data of the compounds are shown in Table I.

N-Alkyl Amidodifluoroarsenites

Starting from 0.2 mole of the corresponding primary amine (ethyl-, *i*-propyl-, or *t*-butyl-amine) and 13.2 g (0.1 mole) arsenic trifluoride, the preparations were carried out in the same manner as that described for N,N-dialkyl amidodifluoroarsenites. After

the solvent was removed by distillation, the raw product remaining was fractionated in vacuum. The N-ethyl- and N-*i*-propyl-imidofluoroarsenites were obtained as almost colorless and odorless liquids. The N-*t*-butyl imidofluoroarsenite solidified to white crystals. Physical and analytical data and the yields of the compounds prepared are shown in Table II.

N-Cyclohexyl Amidodifluoroarsenites

Benzene solutions of 19.8 g (0.2 mole) cyclohexylamine and 13.2 g (0.1 mole) arsenic trifluoride were reacted in the manner used with previous examples. After being filtered by suction, the cyclohexylamine hydrofluoride was washed with benzene. The filtrate containing the main product was distilled. At first benzene was distilled over and then at 95° C/9 mm N-cyclohexyl amidodifluoroarsenite, which solidified to white crystals melting at 65–66° C. Further data are shown in Table I.

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THE SYNTHESIS OF SOME INDOLYLALKYLAMINOALCOHOLS¹

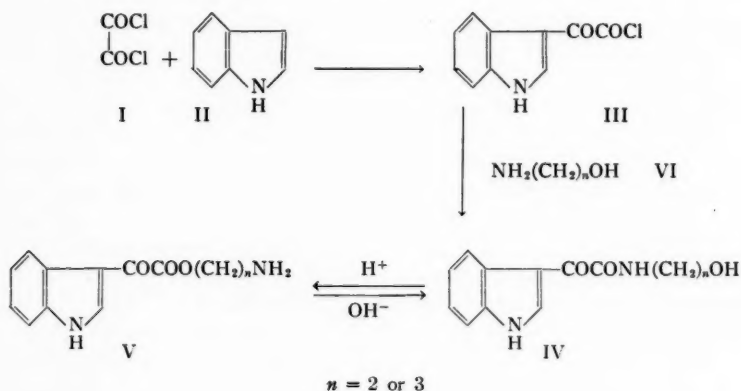
GERASSIMOS FRANGATOS, GEZA KOHAN, AND FRANCIS L. CHUBB

ABSTRACT

A series of 3-indolylalkylaminoalcohols have been obtained from the lithium aluminum hydride reduction of the amides prepared by the reaction of 3-indoleglyoxylyl chloride and 2-methyl-3-indoleglyoxylyl chloride with primary aminoalcohols. When acetone was used as solvent in the reaction of 3-indoleglyoxylyl chloride and either 2-aminoethanol or 3-aminopropanol, the solvent participated in the reaction resulting in the formation of 2,2-dimethyl-3-(3-indoleglyoxylyl)oxazolidine and 2,2-dimethyl-3-(3-indoleglyoxylyl)tetrahydro-1,3-oxazine respectively. When the latter two compounds were reduced by lithium aluminum hydride, both carbonyl groups were completely reduced and reductive cleavage of the oxazolidine and tetrahydro-1,3-oxazine rings occurred to form the corresponding open-chain alcohols.

It has been shown (1) that oxalyl chloride (I) reacts readily with indole (II) to form 3-indoleglyoxylyl chloride (III), which in turn reacts with amines to give the corresponding amide. Lithium aluminum hydride reduction of these amides resulted in the synthesis of a variety of substituted or unsubstituted tryptamines, except in a few cases (2, 3), where hydroxyamines were isolated from the reaction mixture, because of partial reduction of the carbonyl group to a carbinol instead of to a methylene group.

As part of a program leading to the synthesis of basic esters (4) related in structure to reserpine, the reaction of III with 2-aminoethanol and 3-aminopropanol was investigated. When III was added to a dioxane solution of a slight excess of the aminoalcohol, the corresponding amide IV was obtained in excellent yield. An excess of the aminoalcohol was necessary to prevent the rearrangement (5) of the amide to the isomeric ester V or even simultaneous formation of V. Thus when the aminoalcohols VI were added to III, the amides IV were obtained but apparently were contaminated by the isomeric esters. Lithium aluminum hydride reduction of the amides, carried out in boiling dioxane with a large excess of lithium aluminum hydride, gave the corresponding indolylalkylamines as distillable oils, listed in Table I.



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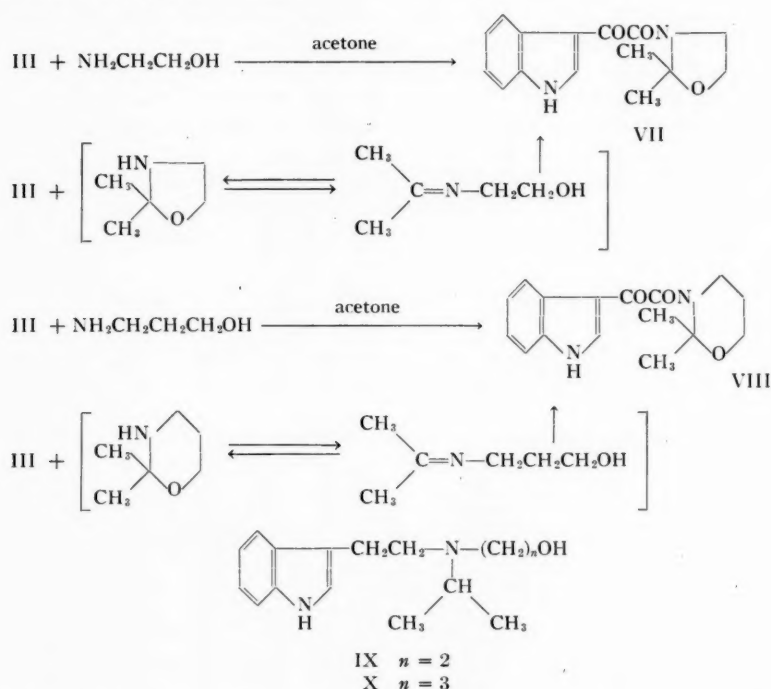
Contribution from the Research Laboratories, Frank W. Horner Limited, Montreal, Que.

TABLE I
Indoleglyoxylamides and indolylalkylaminoalcohols

No.	Structure	Yield, %	Derivative	M.p., °C	B.p., °C	Molecular formula	Analyses					
							Calculated, %			Found, %		
							C	H	N	C	H	N
	$R_1 =$		$R_2 =$			$R_3 =$						
(1)	$R_1\text{COCOONHCH}_2\text{CH}_2\text{OH}$	79.0		213		$\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3$	62.06	5.21	12.07	61.77	5.29	12.02
(2)	$R_1\text{COCOONHCH}_2\text{CH}_2\text{CH}_2\text{OH}$	68.3		212		$\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3$	63.40	5.72	11.38	63.03	5.86	11.40
(3)	$R_1\text{COCOR}_3$	74.5		208		$\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3$	66.16	5.92	10.29	65.84	6.12	10.06
(4)	$R_1\text{COCOR}_4$	68.6		216		$\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3$	67.11	6.33	9.79	67.32	6.38	9.94
(5)	$R_1\text{CH}_2\text{CH}_2\text{N}(\text{CH}(\text{CH}_3)_2)\text{CH}_2\text{CH}_2\text{OH}$	56.0	Hydrochloride	182		$\text{C}_{20}\text{H}_{28}\text{N}_2\text{O}$	63.70	8.20	9.91	63.74	8.16	9.62
(6)	$R_1\text{CH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{CH}_2\text{OH}$	72.0	Picrate	146	210/1 mm	$\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3$	53.05	5.30	14.73	53.52	5.44	14.84
(7)	$R_1\text{CH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{OH}$	64.5	Hydrochloride	122		$\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3$	61.30	7.46	11.02	61.11	7.41	11.15
			Picrate	163		$\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3$	51.00	4.73	15.65	51.00	4.92	16.06
			Hydrochloride	148		$\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3$	59.86	7.12	11.64	60.06	7.07	11.53
(8)	$R_1\text{CH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{CH}_2\text{OH})_2$	48.8		128		$\text{C}_{18}\text{H}_{24}\text{N}_2\text{O}$	73.80	9.29	10.76	73.44	9.35	10.80
(9)	$R_2\text{C}(\text{O})\text{C}(\text{O})\text{NHCH}_2\text{CH}_2\text{OH}$	71.0		168		$\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_3$	63.40	5.72	11.38	63.34	5.81	11.20
(10)	$R_2\text{C}(\text{O})\text{C}(\text{O})\text{NHCH}_2\text{CH}_2\text{CH}_2\text{OH}$	69.2	Monohydrate	104		$\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_3 \cdot \text{H}_2\text{O}$	60.42	6.52	10.07	60.57	6.38	10.42
(11)	$R_2\text{CH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{CH}_2\text{OH}$	58.0	Picrate	121	205/0.5 mm	$\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3$	71.52	8.31	12.84	71.29	8.33	13.10
(12)	$R_2\text{CH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{CH}_2\text{OH}$	53.7	Hydrochloride	172		$\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3$	51.00	4.73	15.65	51.13	4.83	15.70
			Picrate	176		$\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3$	62.55	7.88	10.42	62.63	7.88	10.45
			Picrate	181		$\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3$	52.06	5.02	15.18	52.37	5.25	14.60

When acetone was used as a solvent in the reaction of III with 2-aminoethanol and 3-aminopropanol it was found that the amides obtained were different from those obtained when dioxane was used as the solvent. Analysis and infrared spectra showed that acetone had participated in the reaction to furnish a substituted oxazolidine VII and tetrahydro-1,3-oxazine VIII respectively. The infrared spectrum of these compounds exhibited a triplet of bands in the $1020\text{--}1210\text{ cm}^{-1}$ region, characteristic of the oxazolidine (6) and 1,3-tetrahydrooxazine (7) rings while hydroxy group absorption was absent. Additional supporting evidence was provided by the fact that both compounds VII and VIII were obtained from the reaction of III with the preformed condensation products of acetone and either 2-aminoethanol or 3-aminopropanol. It has been shown (8, 9) that the reaction product of 2- or 3-primary aminoalcohols and aliphatic ketones is a mixture of either oxazolidine or tetrahydro-1,3-oxazine and the corresponding Schiff base in a state of mobile equilibrium. However, when a substituent other than hydrogen is attached to the nitrogen, this state of equilibrium no longer exists because the Schiff base cannot form and only the oxazolidine or tetrahydro-1,3-oxazine structure remains.

When VII and VIII were subjected to lithium aluminum hydride reduction in boiling dioxane, both carbonyl groups were completely reduced and reductive cleavage of the oxazolidine and tetrahydro-1,3-oxazine rings occurred to give the open-chain alcohols IX and X, respectively. This reductive cleavage was in agreement with earlier reports (10) on the cleavage of oxazolidines.



2-Methyl-3-indoleglyoxylyl chloride (XI) reacted with 2-aminoethanol and 3-aminopropanol in dioxane to give the corresponding amides. The latter compounds were

reduced by lithium aluminum hydride to the corresponding 2-methyl-3-indolyethyl-aminoalcohols (see Table I).

An attempt to effect the reaction of XI with 2-aminoethanol and 3-aminopropanol in acetone solution or with the preformed condensation products of acetone and 2-aminoethanol or 3-aminopropanol only resulted in the formation of tars. Molecular models (Stuart) of the expected compounds showed that the hindrance was not purely steric.

EXPERIMENTAL*

3-Indoleglyoxylyl Chloride

The procedure of Nogradi (11) was followed for the preparation of this compound. 2-Methyl-3-indoleglyoxylyl chloride was similarly prepared.

2-(3-Indoleglyoxyl)amidoethanol

Freshly prepared 3-indoleglyoxylyl chloride (29.5 g) was suspended in 125 ml of dioxane and cooled to 15°. This suspension was added slowly with stirring to a solution of 25 ml of 2-aminoethanol in 100 ml of dioxane. During the addition and for another half hour, the reaction was kept at 12–15°. Most of the dioxane (175 ml) was distilled under reduced pressure and 150 ml of water was added to the mixture. A yellowish coarse powder precipitated, which was filtered and air-dried. Recrystallization from ethanol yielded 26 g (79%), m.p. 213°.

2-(3-Indolyethyl)aminoethanol

Nine grams of 2-(3-indoleglyoxyl)amidoethanol was dissolved in 350 ml of dry dioxane. This solution was added with mechanical stirring and under an atmosphere of dry nitrogen to a suspension of 12.5 g of pulverized lithium aluminum hydride in 230 ml of boiling dioxane. The solution was added at such a rate as to maintain refluxing of the reaction mixture without external heating. After the addition was over the heating was resumed. Great care had to be exercised during the first hour of refluxing because the reaction mixture occasionally started to foam badly. At this point heating and stirring were discontinued for a short time. After the foaming ceased the mixture was refluxed for 6 hours and cooled. The excess lithium aluminum hydride was destroyed cautiously with wet dioxane. The reaction mixture was again brought to the boiling point and filtered hot. The filter cake was washed with 50 ml of hot dioxane. The combined clear filtrates were distilled under reduced pressure and the residual oil was distilled *in vacuo*. 2-(3-Indolyethyl)aminoethanol (5.2 g, 64.5%) was obtained distilling at 205°/0.2 mm. A chloroform solution of this compound was treated with dry hydrogen chloride and the corresponding hydrochloride precipitated. It was recrystallized from a minimum amount of methanol and melted at 148°.

The amides and aminoalcohols listed in Table I (Nos. 2, 6, 9, 10, 11, 12) were prepared in the same way as 2-(3-indoleglyoxyl)amidoethanol and 2-(3-indolyethyl)aminoethanol.

2,2-Dimethyl-3-(3-indoleglyoxyl)oxazolidine

(A) Fifty grams of 2-aminoethanol was dissolved in 500 ml of acetone at 0°. To this solution a suspension of 50 g of 3-indoleglyoxylyl chloride was added slowly with stirring. The reaction mixture was cooled and stirred for an additional half hour. The yellow color of the suspension gradually faded and an oily layer separated at the bottom of the flask. The acetone was distilled under reduced pressure. The viscous residue was dissolved in

*Melting points are uncorrected. Analyses were determined by E. Thommen, Basel, Switzerland. Infrared spectra were obtained in a Perkin-Elmer 21 double-beam spectrophotometer using sodium chloride optics in potassium bromide disks.

100 ml of boiling ethanol, treated with charcoal, and precipitated upon addition of water. 2,2-Dimethyl-3-(3-indoleglyoxyl)oxazolidine (36.5 g, 62.3%) was obtained, m.p. 208°. It exhibited a triplet absorption band in the infrared at 1104, 1131, and 1171 cm^{-1} .

(B) "2,2-Dimethyloxazolidine" was prepared according to the directions of Bergmann (9). Thirty-seven grams of freshly prepared "2,2-dimethyloxazolidine" was dissolved in 500 ml of absolute ether. To this mixture a suspension of 32 g of 3-indoleglyoxylyl chloride in 250 ml of ether was added at room temperature with stirring. After the addition was completed the reaction mixture was stirred and refluxed gently for 20 minutes. It was cooled and filtered. The crude product was washed on the filter with water and recrystallized from aqueous ethanol. Twenty-eight grams (74.5%) of 2,2-dimethyl-3-(3-indoleglyoxyl)oxazolidine was obtained melting at 208° and showing no depression of melting point upon mixing with a sample obtained according to procedure A.

2-(3-Indolyethyl)isopropylaminoethanol

The reduction of 2,2-dimethyl-3-(3-indoleglyoxyl)oxazolidine was effected by lithium aluminum hydride in boiling dioxane. The procedure already described for the synthesis of 2-(3-indolyethyl)aminoethanol was followed. It exhibited infrared absorption bands at 3538 (OH) and 3252 cm^{-1} (NH) (12).

2,2-Dimethyl-3-(3-indoleglyoxyl)tetrahydro-1,3-oxazine

This compound was obtained from the reaction of 3-indoleglyoxylyl chloride with either 3-aminopropanol in acetone solution or "2,2-dimethyltetrahydro-1,3-oxazine" (7). Similar experimental conditions to those used for the synthesis of 2,2-dimethyl-3-(3-indoleglyoxyl)oxazolidine (procedures A and B). It exhibited a triplet absorption band in the infrared at 1067, 1105, and 1148 cm^{-1} .

3-(3-Indolyethyl)isopropylaminopropanol

The lithium aluminum hydride reduction of 2,2-dimethyl-3-(3-indoleglyoxyl)tetrahydro-1,3-oxazine to 3-(3-indolyethyl)isopropylaminopropanol was effected by a procedure similar to that used for the reduction of 2-(3-indoleglyoxyl)aminoethanol.

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ABSORPTION SPECTRA OF 2,5-DIMERCAPTO-1,3,4-THIADIAZOLE AND ITS METHYL DERIVATIVES¹

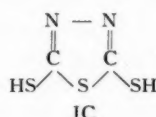
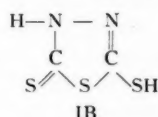
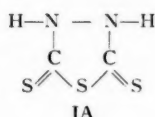
G. D. THORN

ABSTRACT

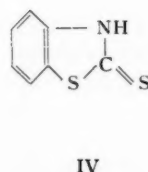
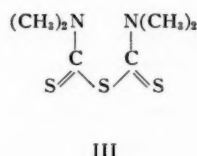
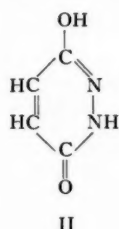
The absorption spectra of the three tautomeric forms of 2,5-dimercapto-1,3,4-thiadiazole have been determined by using the N- and S-methyl derivatives. In the ultraviolet region, a hypsochromic shift in absorption maxima is shown in the change from the dithionic to the thionic-thiolic and to the dithiolic forms. Strong bands in the infrared at 1508–1475 cm⁻¹

and 1435–1415 cm⁻¹ have been assigned to $\text{>N}-\text{C}=\text{S}$ and $-\text{N}=\text{C}-\text{S}-$, respectively.

Theoretically the title compound can exist in any of three tautomeric forms (IA, IB, or IC) and thus the name 2,5-dimercapto-1,3,4-thiadiazole may be too rigid. An analogy exists in maleic hydrazide, for which the structure II has been assigned (1), and from which the various N- and (or) O-methyl derivatives have been obtained by alkylation under varied conditions. Zahradník (2) has obtained the ultraviolet absorption spectrum of dimercaptothiadiazole, and has designated the structure as being that of form IA. Sheinker *et al.* (3) believe the compound to have a mixed thionic-thiolic structure (IB).



Substitution of alkyl groups for SH or NH hydrogen in 2,5-dimercapto-1,3,4-thiadiazole forces the molecule into one of the tautomeric forms IA, IB, or IC. An investigation of the ultraviolet and infrared spectra of the various alkyl-substituted derivatives was made therefore with a view to assigning specific molecular structures to the various absorption bands of the parent compound.



The dithiocarbamate grouping, as in esters of dithiocarbamic acids, or in tetramethylthiuram monosulphide (III), shows strong ultraviolet absorption bands in the regions 275–290 mμ and 245–260 mμ (both with log ε about 4), and weaker absorption in the region 325–360 mμ (log ε about 1.8) (see, for example, Janssen (4)). Zahradník (2)

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Contribution No. 174, Pesticide Research Institute, Canada Department of Agriculture, University Sub P.O., London, Ontario.

observed that dimercaptothiadiazoledid not follow this pattern, but instead showed strong absorption at 332 m μ (log ϵ 4.2, in ethanol) and a weaker absorption band at 265 m μ . This "anomalous" behavior was also seen in the spectrum of mercaptobenzo-thiazole (IV), and was explained on the basis of the —S—C— groups giving the ring a



pseudoaromatic character. With tetramethylthiuram monosulphide (III), where the nitrogens are not joined to form a heterocyclic ring, the expected absorption maximum at 280 m μ is observed.

EXPERIMENTAL

2,5-Dimercapto- and *2-mercapto-5-methylmercapto-1,3,4-thiadiazole* (I and IV, respectively) were prepared according to Thorn and Ludwig (5).

2,5-Dimethylmercapto-1,3,4-thiadiazole (VI) was prepared by the reaction of the dimercaptothiadiazoledid in aqueous ethanol with stoichiometric amounts of methyl iodide and potassium hydroxide, according to Busch and Ziegele (6). Fractional distillation of the water-insoluble product gave a colorless liquid, b.p. 87–88° at 0.05 mm; $n_{23.5}^D$ 1.6530. Calc. for $\text{C}_4\text{H}_6\text{N}_2\text{S}_3$: S, 54.0%. Found: S, 54.1%. Busch and Ziegele (6) record a melting point of 136°, but in this laboratory a solid product was not obtained in any of several preparations.

2-Mercapto-4-methyl-1,3,4-thiadiazoline-5-thione (VII) was obtained from methylhydrazine and CS_2 according to the method of Busch and Ziegele (7). The product melted at 65–66° after crystallization from diethyl ether. Busch and Ziegele (7) record a melting point of 69°. Calc. for $\text{C}_2\text{H}_4\text{N}_2\text{S}_3$: S, 58.6%. Found: S, 58.6%.

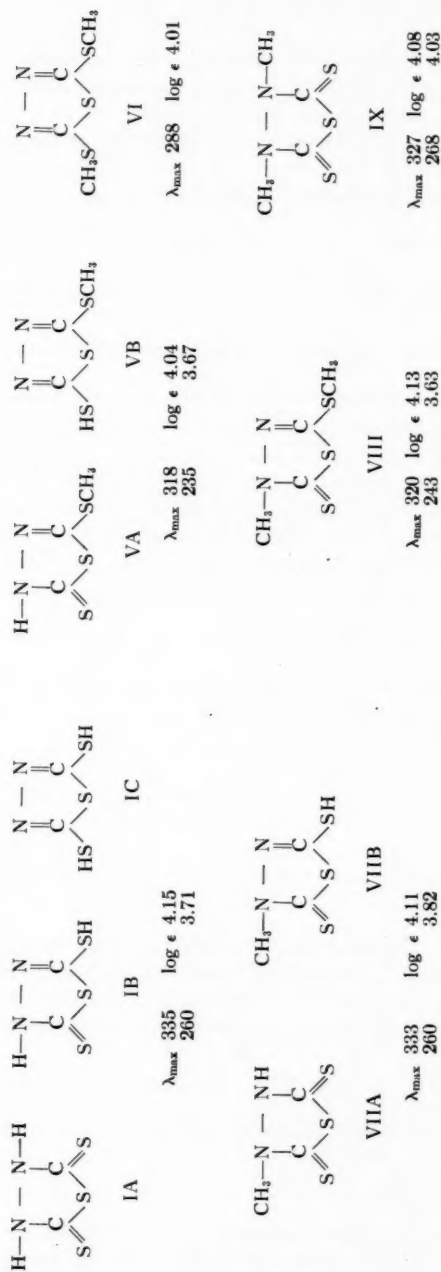
2-Methylmercapto-4-methyl-1,3,4-thiadiazoline-5-thione (VIII) was prepared from VII according to Busch and Ziegele (7) and melted at 81–82° after crystallization from 95% ethanol. Lit. (7) gives a melting point of 88°. Calc. for $\text{C}_4\text{H}_6\text{N}_2\text{S}_3$: S, 54.0%. Found: S, 53.8%.

3,4-Dimethyl-1,3,4-thiadiazolidine-2,5-dithione (IX) was prepared by heating under reflux for 9 hours an alcohol solution of stoichiometric amounts of dimethylhydrazine dihydrochloride, potassium hydroxide, and carbon disulphide. The product was precipitated from the reaction mixture by the addition of water; yield, 50%. The melting point was 168–169°, after crystallization from 95% ethanol. Calc. for $\text{C}_4\text{H}_6\text{N}_2\text{S}_3$: S, 54.0%. Found: S, 53.7%.

Ultraviolet absorption spectra were measured in ethanol solution with the Beckman DK-1 spectrophotometer. Infrared spectra were recorded with the Perkin-Elmer Model 21 instrument with NaCl prism, in chloroform solution or KBr disk.

DISCUSSION

The various tautomeric structures for the dimercaptothiadiazoledid derivatives studied are given in Fig. 1, together with the ultraviolet absorption bands of these compounds. Nearly identical spectra (λ_{max} 327–335 and 260–268 m μ) are shown by compounds I, VII, and IX. This absorption thus establishes the thione structure for these compounds, as in IX the possibility of enethiolization does not exist. Forcing one of the thiocarbamoyl groups into the enethiol form as in V and VIII results in a hypsochromic shift of both absorption bands. The similarity in spectra for these latter two compounds suggests that in V the second thiocarbamoyl group is in the thione form. The fixing of both thiocarbamoyl groups into the enethiol arrangement results in a further hypsochromic shift



of the band of longer wavelength, with loss, in the region studied, of the shorter wavelength band.

Thus, on a consideration of ultraviolet absorption spectra alone, definite assignments of structure can be made. A study of the infrared absorption spectra, however, suggests that these assignments are not as categorical as given above.

The strong band in the region 1610–1470 cm^{-1} appearing in the spectra of compounds

containing the $\text{>N-C}\begin{smallmatrix} \text{S} \\ \text{//} \end{smallmatrix}$ group has been assigned by Randall *et al.* (8) to a ν_{CN} frequency strengthened by the ionic form $\text{>N}-\overset{+}{\text{C}}-\text{S}^-$, and was termed by these authors as a

“thioureide ion” band. Chatt *et al.* (9), however, have assigned this band to the contri-

bution by the canonical form $\text{>N}^+=\text{C}\begin{smallmatrix} \text{S}^- \\ \text{//} \end{smallmatrix}$, in the case of dithiocarbamate esters and

heavy metal complex salts, and have restricted the “thioureide ion” band to the region 1542–1480 cm^{-1} . Other workers (10, 11, 12) have concluded that this thioureide band is due to a δ_{NH} frequency. An appraisal has been made by Elmore (13) of the nature of the thioureide band. Elmore has suggested that since this band occurs with compounds having no NH group, it cannot be entirely due to a δ_{NH} vibration, although he postulated that coupling between δ_{NH} and ν_{CN} modes may occur in some instances. Lieber *et al.* (14) on the basis of the spectra of a number of 1-substituted tetrazolinethiones and 4-substituted semicarbazides have made a frequency assignment of 1555–1474 cm^{-1} for the

>N-C(=S)- grouping and 1395–1338 cm^{-1} for the >C=S linkage. Lieber *et al.* (14)

used the occurrence of these bands in 1-substituted tetrazolines (X) together with the absence of the SH band in the region 2600–2550 cm^{-1} (15) to support the thione rather than the thiol structure for these compounds.

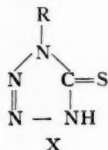


Table I summarizes the important bands observed for the dimercaptotriadiazoles. In all but two of the compounds, two strong bands, at 1435–1415 cm^{-1} and 1508–1475 cm^{-1} (chloroform solution), are observed. The former is not given by compound IX, the latter not by compound VI. The above results lead us to the view that the 1508–1475

cm^{-1} is indeed assignable to the $\text{>N-C}\begin{smallmatrix} \text{S} \\ \text{//} \end{smallmatrix}$ grouping, perhaps modified by resonance

as suggested by Chatt *et al.* (9), and that the band at 1435–1415 cm^{-1} is associated with the $\text{>N}=\text{C}\begin{smallmatrix} \text{S}^- \\ \text{//} \end{smallmatrix}$ grouping.

Lieber *et al.* have made a frequency assignment of 1395–1338 cm^{-1} for the $\text{C}=\text{S}$ linkage. Mecke and Mecke (16) and Mecke *et al.* (12) had previously assigned a band of strong intensity in the region 1200–1050 cm^{-1} to the $\text{C}=\text{S}$ grouping, and a band in the 1350–1300 cm^{-1} region to CN vibration. In the dimercaptotriadiazoles, a strong band

is given by chloroform solution of all the compounds studied, including the S,S'-dimethyl ether (V), in the 1395–1338 cm^{-1} region assigned by Lieber *et al.* to C=S. An exception is that dimercaptothiadiazoole itself does not show absorption in this region in the KBr disk. Strong bands are given also by all these compounds in Mecke's 1050–1200 cm^{-1} region. It may be mentioned that for the methyl and ethyl esters of N,N-dimethyl- and N-methyl-dithiocarbamic acid and of dithiocarbamic acid itself, a strong band is seen (17) in the region 1385–1345 cm^{-1} , but that strong absorption is shown in the 1200–1050 cm^{-1} region only by those dithiocarbamates substituted in the nitrogen, and not by ethyl or methyl dithiocarbamate. On the basis of the above, the author tends to the assignment of Lieber *et al.* of 1395–1338 cm^{-1} for C=S when forming part of the thioureide grouping, made tentative, however, by the two anomalies mentioned in the dimercaptothiadiazoole compounds. The thiocarbonyl stretching frequency has been assigned recently to the region 1220–1080 cm^{-1} by Spinner (18), on the basis of unambiguous identity in such compounds as thioformaldehyde and thiocarbonyl chloride. Haszeldine and Kidd (19) previously had given the $\nu_{\text{C}=\text{S}}$ vibration as 1078 cm^{-1} for ethylene trithiocarbonate. Thus, as is pointed out by Jones *et al.* (20), the frequency for C=S is dependent on the structural environment and falls within the wide range 1400–1000 cm^{-1} .

Mention was made in the discussion on the ultraviolet absorption spectra of the dimercaptothiadiazoole derivatives that the assignment of structure made was perhaps too rigorous. The infrared spectra of compounds I and VII in chloroform solution made it apparent that these compounds possess an SH group (absorption in the 2600–2550 cm^{-1} region (15)). The postulate may be advanced that in concentrated chloroform solution these two compounds are primarily in the form of structures IB and VIIB, whereas in dilute alcohol solution the dithione structures IA and VIIA are the predominant forms. For structural systems of this type it has been found that a change in medium may alter the tautomeric equilibrium position (see Spinner (20) and references quoted by him).

ACKNOWLEDGMENTS

The author is grateful for the discussions with Robert W. White on the infrared absorption spectra and expresses his thanks to Dorle Bongart for microanalyses and to Marilyn Coleman for technical assistance.

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ARYLPYRIDINES

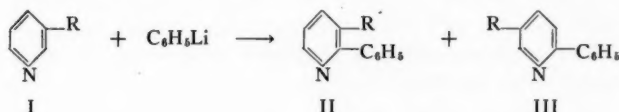
PART II. REACTION OF PHENYLLITHIUM WITH 3-METHOXY- AND 3-AMINO-PYRIDINE^{1,2}

R. A. ABRAMOVITCH AND A. D. NOTATION

ABSTRACT

Phenyllithium has been shown to react with 3-methoxy- and 3-amino-pyridine to give exclusively 3-methoxy-2-phenylpyridine and 3-amino-2-phenylpyridine respectively. The orientation of the products has been established unambiguously. None of the 2,5-isomer was detected in either case. An explanation for this unique orientation is suggested.

In Part I of this series (1) the orientation of the entering phenyl substituent in the addition of phenyllithium to 3-picoline and to nicotine was studied. In the first case the main product was 3-methyl-2-phenylpyridine (II; R = CH₃) together with a small amount of 5-methyl-2-phenylpyridine (III; R = CH₃), the ratio of the isomers being 19:1. On the other hand phenylation of nicotine gave 2-phenyl- (II; R = -α-C₄H₇NCH₃) and 6-phenyl-nicotine (III; R = -α-C₄H₇NCH₃) in a 1:1 ratio. Evidence that the 3-substituent exerts an appreciable steric effect in the end product of the addition was



also presented. The results were interpreted to mean that addition of phenyllithium to 3-substituted pyridines occurs preferentially at the 2-position but that the 3-substituent, if sufficiently bulky, could exert a steric effect resulting in appreciable addition at the 6-position also.

The present paper gives an account of the extension of this study to 3-amino- and 3-methoxy-pyridines both of which are readily available and the products from which could serve as valuable intermediates in synthetic work. Molecular models indicate that the steric effect of a methoxyl group would be expected to be less than that of a methyl group whereas that of a primary amino group, particularly as its lithium salt, should be comparable with that of a methyl group. 3-Methoxypyridine was prepared by methylation of 3-hydroxypyridine according to Prins's procedure (2).

3-Aminopyridine (I; R = NH₂) was treated with a 3-molar excess of phenyllithium to give a 24.5% yield of product. That probably only a single isomer was present was indicated by vapor phase and by column chromatography, and that this isomer was 3-amino-2-phenylpyridine (II; R = NH₂) was shown by comparison of the base and of its picrate with authentic specimens prepared unambiguously from 3-methyl-2-phenylpyridine (3). No evidence for the presence of any 5-amino-2-phenylpyridine in the mixture could be obtained.

In a similar manner, 3-methoxypyridine reacted with phenyllithium to give a 21.2% yield of product C₁₂H₁₁ON. Once again this was shown chromatographically to consist

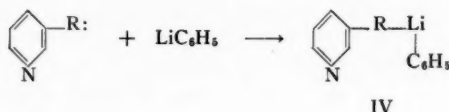
¹Manuscript received March 10, 1960.

Contribution from the Department of Chemistry, University of Saskatchewan, Saskatoon, Saskatchewan.

²Part I: *Can. J. Chem.* **38**, 761 (1960).

of a single isomer which proved to be 3-methoxy-2-phenylpyridine. This could be established quite readily by demethylation to 3-hydroxy-2-phenylpyridine, an authentic specimen of which was obtained from the above 3-amino-2-phenylpyridine. The physical properties of the phenol corresponded also to those reported for 3-hydroxy-2-phenylpyridine (II; R = OH) by Leditschke (4). The infrared spectrum of 3-methoxy-2-phenylpyridine exhibited a band at 1584 cm^{-1} which has been shown to be characteristic of such 2,3-disubstituted pyridine derivatives (5). Once again no 5-hydroxy-2-phenylpyridine was detected in the crude reaction product.

It would seem, therefore, that in the present instance the entering phenyl group is directed *exclusively* to the 2-position. A possible explanation of this observation is that in both the examples studied here the 3-substituent has a pair of electrons which can co-ordinate with the lithium atom to form a complex such as IV in which the phenyl group would be suitably oriented for attack at the 2-position. This, together with the already established tendency for preferential addition to the 2-position (1), would account for the fact that no 6-substitution was observed. Stereospecificity in the addi-



tion of phenyllithium to α -hydroxyketones has been similarly attributed to the formation of a lithium complex as an intermediate (6).

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were measured using a Perkin-Elmer Model 21 instrument and the vapor phase chromatographic work was carried out using a Beckman GC-2 unit with helium as the carrier gas.

Reaction of Phenyllithium with 3-Aminopyridine

Lithium (1.65 g) was finely cut and suspended in anhydrous ether (50 ml) under dry nitrogen. Bromobenzene (11.4 ml; 17 g) in anhydrous ether (20 ml) was added dropwise at such a rate as to maintain gentle reflux. When the formation of phenyllithium was complete 3-aminopyridine (4 g) in anhydrous ether (80 ml) was added over a period of 20 minutes during which time a brilliant yellow suspension was formed. The ether was distilled off and simultaneously replaced by dry toluene (100 ml) and the temperature was raised to the boiling point. The mixture was boiled under reflux with stirring for $7\frac{1}{2}$ hours during which time the color turned a dark brown. Water was carefully added to the cold suspension, the toluene layer separated, and the aqueous layer extracted repeatedly with ether. The combined ether and toluene layers were extracted with dilute hydrochloric acid, the acid extract made strongly basic with sodium hydroxide, and the product extracted with ether. The ether layer was dried (Na_2SO_4), evaporated, and the residue distilled under vacuum to give crude 3-amino-2-phenylpyridine (1.5 g). This was redistilled and obtained as a pale yellow oil, b.p. $119\text{--}121^\circ/0.35\text{ mm}$, which solidified on cooling and was recrystallized from benzene-light petroleum (b.p. $40\text{--}60^\circ$) giving colorless crystals, m.p. $62\text{--}64^\circ$. Calc. for $\text{C}_{11}\text{H}_{10}\text{N}_2$: C, 77.62; H, 5.92. Found: C, 77.90; H, 5.78. Infrared spectrum (Nujol mull) (main peaks only): 3350 (m) (br) , 3220 (m) (br) , 1620 (s) (br) , 1585 (s) , 798 (s) , 743 (s) , 730 (w) , $695\text{ cm}^{-1}\text{ (w)}$.

The monopicrate, on recrystallization from ethanol, had a melting point of 204–206°. Calc. for $C_{11}H_{10}N_2$, $C_6H_5O_7N_3$: C, 51.13; H, 3.28. Found: C, 51.18; H, 3.17.

A sample of crude reaction product (0.1193 g) was chromatographed on a narrow column of alumina (5 g). Elution was carried out using the following sequence of solvents: light petroleum (b.p. 40–60°), benzene – light petroleum, benzene, benzene–ether, ether, ether–methanol, and finally methanol. Only a single colorless band, exhibiting blue fluorescence under ultraviolet light was eluted, and this with benzene–ether. Different portions of the benzene–ether eluate were converted to the picrate. In each case, only 3-amino-2-phenylpyridine picrate, m.p. 204–206°, was obtained. Also, the individual fractions had identical infrared spectra. The total recovery from the column was 0.1018 g. The mixed melting point of the picrate with that of an authentic sample (3) was undepressed. Also, the infrared spectrum of the free base was identical with that of the authentic sample. Only one peak was observed on vapor phase chromatography of the crude free base under a variety of conditions.

Reaction of Phenyllithium with 3-Methoxypyridine

Phenyllithium was prepared from lithium (0.5 g) and bromobenzene (5.7 g) in anhydrous ether. 3-Methoxypyridine (4 g) in anhydrous ether (30 ml) was added dropwise over a period of 20 minutes, after which the ether was distilled off and simultaneously replaced by dry toluene (40 ml). The reaction mixture was stirred and boiled under reflux under an atmosphere of nitrogen for 7 hours, water was carefully added to the cooled suspension, and the toluene layer separated. The aqueous layer was extracted with ether, the combined ether and toluene extracts washed with dilute hydrochloric acid, and the acid solution basified and extracted with ether. The dried (Na_2SO_4) ether extract was evaporated and the residue distilled under vacuum, the fraction (1.4 g), b.p. 120–160°/0.34 mm, being collected. Redistillation gave pure 3-methoxy-2-phenylpyridine, b.p. 110–112°/0.34 mm. Calc. for $C_{12}H_{11}ON$: C, 77.81; H, 5.99. Found: C, 78.13; H, 6.43. Infrared spectrum (liquid film) (main peaks only): 1575 (s), 1265 (s) (br), 1195 (s), 1125 (s), 1015 (s), 795 (s), 735 (s), 692 cm^{-1} (s).

The picrate was recrystallized from ethanol and had a melting point of 153.5–155°. Calc. for $C_{12}H_{11}ON$, $C_6H_5O_7N_3$: C, 52.18; H, 3.41. Found: C, 52.53; H, 3.86.

The crude base was shown to consist of a single compound by column and vapor phase chromatography as described for 3-amino-2-phenylpyridine.

3-Hydroxy-2-phenylpyridine

(i) From 3-Methoxy-2-phenylpyridine

3-Methoxy-2-phenylpyridine (0.2 g) was boiled under reflux for 4 hours with 47% hydrobromic acid (3 ml). The excess hydrobromic acid was then evaporated off and the residue neutralized with 10% sodium carbonate solution and ether extracted. The dried (Na_2SO_4) ether extract was evaporated and the residue of 3-hydroxy-2-phenylpyridine recrystallized from ethanol to give colorless crystals, m.p. 206–207.5°. Leditschke (4) reported a melting point of 205° for this compound. The infrared spectrum of this product was identical with that of an authentic specimen prepared as described under (ii) below. Also, its melting point was undepressed on admixture with the authentic specimen.

(ii) From 3-Amino-2-phenylpyridine

3-Amino-2-phenylpyridine (0.4 g) was dissolved in a mixture of concentrated sulphuric acid (0.8 ml) and water (2 ml). The solution was cooled to 0–5° and diazotized with sodium nitrite (0.3 g) in water (1 ml) and after $\frac{1}{2}$ hour at 0–5° the excess nitrous acid

was decomposed with urea. The solution was then boiled under reflux for 1 hour after which time it gave a negative alkaline β -naphthol test. The reaction mixture was treated with solid sodium carbonate and ether extracted repeatedly. The combined ether extracts were dried (K_2CO_3) and evaporated giving crude 3-hydroxy-2-phenylpyridine (0.35 g) contaminated with some orange impurity. Recrystallization from ethanol gave the pure phenol, m.p. 206–207.5°. Infrared spectrum (Nujol mull) (main peaks only): 1573 (m), 1280 (s) (br), 1182 (s), 1115 (m), 802 (m), 735 (s), 693 cm^{-1} (m).

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THE ATTACK OF CHROMITE BY SULPHURIC ACID¹

W. J. BIERMANN AND MENNO HEINRICH

ABSTRACT

A study was made of the attack of a "low grade" chromite concentrate by sulphuric acid of various concentrations with a view toward formulating a more adequate description, or mechanism, of the process. Consideration of available evidence eliminates the possibility of hydrolysis playing an important role in the process. A qualitative mechanism consistent with the available facts is based on an initial protonic attack, followed by formation of various sulphate complexes of chromium.

INTRODUCTION

The utilization of chromites which are currently classed as "low grade", due, in great measure, to the large amount of contained iron, has been the subject of numerous investigations. These have been comprehensively collected by Udy (1) and an earlier review by Downes and Morgan (2) gives an excellent critical recount of efforts directed toward development of the North American deposits. Methods based on sulphuric acid leaching figure prominently in these reviews.

The present work started as a simple attempt to establish conditions required for the complete conversion of chromite concentrate to a soluble product by sulphuric acid digestion, preparatory to other studies. After a few experiments it became obvious that the attack of chromite by sulphuric acid was not a simple process, and the series of experiments described herein was undertaken to give some clarification to the process involved. It is, in a sense, an extension of the leaching experiments at the Mines Branch laboratories, described by Downes and Morgan. Their objective was the establishment of optimum conditions for the removal of iron by treating the chromite with insufficient acid for complete destruction of the chromite lattice. Their conclusion was that only a fixed portion of iron could be removed by leaching, and a mechanism involving hydrolysis of dissolved cations was postulated to explain this limit of beneficiation.

EXPERIMENTAL METHODS

For the rate of attack of chromite by sulphuric acid to be conveniently rapid, it is necessary that the sulphuric acid be somewhat diluted and that the temperature be maintained above the normal boiling point of the solution. A simple steel pressure vessel, sealed by a Teflon "O" ring, was found to be more convenient than the customary sealed glass tubes for containing the reactants. The reactants themselves were placed in an open glass tube, whose upper end was loosely closed by a wisp of glass wool to prevent mechanical spraying of sulphuric acid onto the inner walls of the steel container. A pressure gauge gave a rough measure of the rate of reaction; as sulphuric acid is used up the vapor pressure increases, leveling off to a constant value as the rate of reaction decreases. Experimentally, a known weight of chromite and a weighed amount of sulphuric acid of known concentration were placed in the glass vessel and digested until the constancy of the pressure reading showed that the rate of reaction had slowed down to a negligible value. The contents of the glass tube were then removed and analyzed.

After a digestion of chromite concentrate with sulphuric acid the reaction vessel contained solution, unattacked chromite, and a finely divided insoluble substance; this latter, for lack of a more definitive designation, we have called "altered chromite".

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Contribution from the Department of Chemistry, University of Manitoba, Winnipeg, Manitoba.

The total amount of solid residue was determined by washing with either hot water or dilute sulphuric acid, the amount of residue generally being greater when an acid was used and, under similar washing conditions, reproducible to within a few per cent. Resolution of the total solid into unattacked and altered chromite was hampered by the slow reactivity of the altered chromite. After some experimentation it was found that boiling with two molar sodium hydroxide solutions converted the altered chromite to a readily acid-soluble, gelatinous substance, permitting the isolation of the unattacked chromite by filtration. The weight of altered chromite is the difference between the total residue weight and the excess chromite. Composition of the altered chromite was obtained by analysis of the filtrate from the chromite separation.

The determination of chromium and iron was done with a standard redox titration. Sulphate was determined by precipitation and weighing as barium sulphate. Acetylacetone was added to prevent loss of sulphate by complexation with chromium (III) ions. Aluminium was determined spectrophotometrically by using alizarin red-S in the presence of calcium (3). Shapiro and Brannock (4) have shown that no interferences will result from substances present in these samples. Magnesium was titrated with standard ethylenediaminetetraacetic acid. The amounts of calcium, manganese, and titanium present were too small to have any significant effect on the conclusions reached here and hence were generally ignored.

The chromite used in these experiments was a concentrate prepared from material taken from the Bird River chromite complex and supplied through the courtesy of the Research Department of the Hudson Bay Mining and Smelting Co. This concentrate assayed 41.8% Cr_2O_3 , had a chromium-iron ratio of 1.36 to 1, and the particle size was about 80 mesh.

EXPERIMENTAL RESULTS

Table I shows the weights of the three materials obtained by digestions under a variety of conditions. The amount of sulphuric acid is described in terms of "percentages of equivalence", an equivalent of sulphuric acid being calculated as the amount of sulphuric acid required to convert the concentrate completely to a mixture of normal sulphates. Concentration of sulphuric acid is described by a conventional volume ratio of concentrated sulphuric acid to water.

The data suggest that the amount of chromite unattacked by sulphuric acid is determined primarily by the amount of acid present. When the acid used is about 50% of equivalence, the unattacked chromite is generally quite close to the amount anticipated from stoichiometry, provided sufficient time is allowed for equilibrium to be established. Some silica is dissolved by the sodium hydroxide, accounting for the small apparent excess of attack. In no case was the excess attack great enough to indicate significant regeneration of sulphuric acid by hydrolysis. Figure 1 shows a relationship between the amount of unattacked chromite and the sulphuric acid concentration, most effective attack occurring in the region of equal volumes of sulphuric acid and water. A diminished rate of attack at lower concentration is anticipated in a presumably protonic attack on the chromite lattice; the falling off of rate at higher concentrations is most readily rationalized on a purely mechanical basis because, as shown in Fig. 2, the amount of "altered chromite" begins to increase rapidly at sulphuric acid concentrations higher than 1 to 1.

Selection of data for inclusion in Figs. 1 and 2 was necessary in order to compare runs which differed only in the experimental variables plotted. Examination of runs not

TABLE I
Products formed on sulphuric acid digestion of chromite

Run No.†	Conc. $\text{H}_2\text{SO}_4:\text{H}_2\text{O}$, ml/ml	% equivalence	Temp., °C	Time, hours	Unattacked chromite, g/g*	"Altered chromite", g/g*
1w	1:1	200	250	24	.256	1.76
2w	2:1	200	250	24	.386	1.06
3w	2:1	200	210	21	.105	.193
4w	1:1	200	210	21	.009	.057
5w	1:1.5	200	210	21	.380	.004
6w	1:2	200	210	21	.588	.013
7w	1:1.5	200	200	7.5	.406	.000
8w	1:2	200	200	7.5	.708	.000
9	1:1	100	250	24	.258	
10a	1:2	100	250	19	.362	.228
11w	1:2	100	250	19	.362	.310
12a	2:1	52.5	250	7.5	.477	.320
13w	2:1	52.5	250	7.5	.499	.158
14a	1.5:1	53.1	250	7	.484	.339
15w	1.5:1	53.1	250	7	.508	.189
16a	1:1	53.1	250	6	.424	.454
17w	1:1	53.1	250	6	.433	.458
18a	1:1	53.1	250	7	.424	.522
19a	1:1.5	40.6	250	7.5	.600	.324
20w	1:1.5	40.6	250	7.5	.619	.211
21a	1:1.5	52.5	250	19.5	.452	.419

*The weights of products are grams per gram of chromite in the digestion charge.

†The symbol (w) after the number means that soluble products were removed with hot water; the symbol (a) means that dilute sulphuric acid was used.

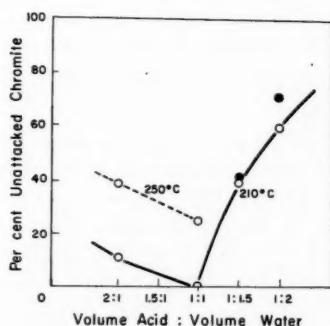


FIG. 1. Degree of attack of chromite as a function of acid concentration. The amount of acid present is 200% of equivalence and the time is 21 hours, except for blackened points which are 7.5 hours and 200° C.

included in these plots discloses no behavior contrary to the conclusions drawn from the data selected.

The dotted portion of Fig. 1 shows that the rate of attack at higher acid concentrations drops as the temperature is increased to 250° C. Comparing runs numbers 1, 2, 3, and 4 in Table I shows how this increase in temperature simultaneously brings about a marked increase in the amount of "altered chromite".

The insoluble material, which we have designated "altered chromite", is formed whenever the acid concentration is high enough to give a reasonable rate of attack on chromite. This, presumably, is the same material which the Mines Branch workers consider to be

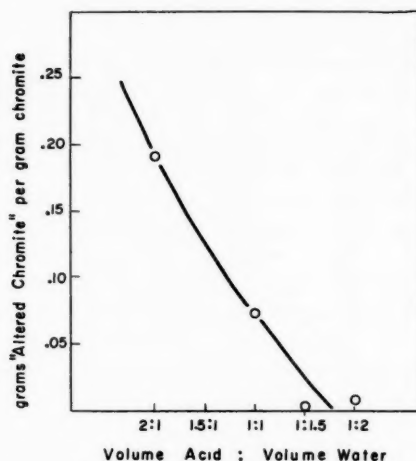


FIG. 2. Formation of "altered chromite" as a function of acid concentration. Acid is 200% of equivalence, time is 21 hours, and the temperature is 200° C.

hydrolysis products of the trivalent ions, but which assumption is not consistent with their observation, substantiated in this work, that the amount of this material increases with sulphuric acid concentration. The physical and chemical properties (finely divided, grey-green, and acid-insoluble) are also suggestive that an alternate explanation is required. Chemical analyses of two representative samples of the "altered chromite" are presented in Table II, and the cation:anion ratio seems to indicate conclusively that

TABLE II
Analysis of typical "altered chromites"

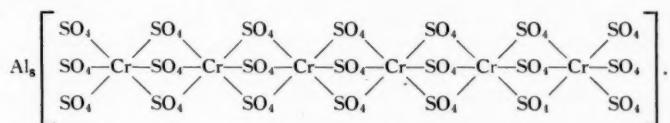
From digestion No.	% Cr	Fe	Al	Mg	SO ₄	Ratio equivalents, cations:anion
18a	7.25	9.56	4.39	1.82	60.0	1.12
2	10.37	6.43	2.42	1.55	68.2	.88

hydrolysis cannot be a significant factor in the formation of the insoluble material. Complete analysis of the products was not generally made, partial analysis of the products showing that the results were quite constant within a given region of acid excess. The slight excess of cation over sulphate was typical of the runs using 50% equivalence of acid. This is ascribed to hydrolysis of the product during the manipulations subsequent to digestion; during extraction of the soluble products the precipitate tended to develop a gelatinous nature, suggestive of an hydroxylation process.

The available facts are better explained on the postulate that the "altered chromite" is a mixture of the hydrogen, aluminum, magnesium, and iron (II) salts of sulphato-polychromate (III) anions. Recoura's work (5), in general confirmed by Whitney (6), substantiates the probability of this explanation, since he reports the preparation of a series of "chromium polysulphuric acids" under conditions similar to the digestion conditions, and observed most of their salts were insoluble and closely resembled the "altered chromite" in appearance. The formation and composition of such polynuclear

complexes will be a function of ligand concentration, central ion concentration (7), and of the relative concentrations of protons and other metals which can function as cations. This is completely consistent with the observation that high sulphate concentrations favor formation of the insoluble compounds, that the percentage of sulphate in these compounds is observed to increase when excess sulphuric acid is used, and that the removal of iron and chromium (III) is lowest with concentrated sulphuric acid, which is also the most favorable condition for formation of these complexes.

To further strengthen this explanation, typical compounds of the type postulated were prepared under similar conditions. By digesting chromium (III) sulphate with sulphuric acid, in a molar ratio of 1 to 4, a water and acid-insoluble substance, whose analysis corresponded closely to $H_2[Cr_2(SO_4)_4]$, separated. On baking until sulphur trioxide fumes ceased to appear, the analysis of the solid corresponds to $H_2[Cr_4(SO_4)_7]$, agreeing in properties and chemical analysis with the product Recoura designated the "isomeric form". Digestion of an equimolar mixture of aluminum and chromium (III) sulphates with excess sulphuric acid gave precipitation of a substance corresponding in analysis to $Al_3[Cr_2(SO_4)_7]_3$. Improbable though this compound first looks, it can be assigned a provisional structure of



This is consistent with the known co-ordination chemistry of chromium (8).

DISCUSSION

The Mines Branch mechanism for the attack of chromite by sulphuric acid would seem to profit by modification to the following scheme. The initial step is a protonic attack of the chromite lattice, bringing the metallic constituents into solution in the same ratio as they occur in the lattice. Precipitation takes place in a second step. Sulphato complexes of chromium (III) are formed and, under conditions of sufficiently high concentration of chromium (III) ions and sulphate ions, these will include various anionic polynuclear species whose hydrogen or other salts are insoluble. Increasing temperature also favors formation of these polynuclear products. Attack of the chromite may become very slow after accumulation of these insoluble salts, hence the failure to complete the decomposition of the chromite in a reasonable time when excess of sulphuric acid is used.

The more obvious weaknesses of the hydrolysis theory are: first, the precipitated iron is almost completely in the form of iron (II) which is not easily hydrolyzable; second, precipitation takes place when large amounts of unused acid are present; and, third, hydrolysis cannot account for the fact that the percentage of insoluble products increases as the concentration of sulphuric acid increases.

A quantitative description of the over-all process requires considerably more knowledge of the sulphato polychromium (III) complexes, particularly equilibrium constant information, than is now available. Such information we hope will be forthcoming in part, as a result of continued work on the chemistry of chromite in this laboratory.

Metallurgically, this work makes a somewhat negative contribution to substantiating the observation that there is a limit to the amount of iron removal possible from untreated chromite by sulphuric acid leaching. A second fact, that the percentage of chromium

convertible from chromite to insoluble polynuclear forms can be varied over a wide range by altering the concentration and temperature of the leaching acid, is an observation whose metallurgical significance cannot be assigned until the chemistry of these compounds is further explored.

ACKNOWLEDGMENTS

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QUANTITATIVE ANALYSIS OF COMBUSTION PRODUCTS BY GAS CHROMATOGRAPHY

THE OXIDATION OF A RICH *n*-PENTANE-AIR MIXTURE IN A FLOW SYSTEM¹

S. SANDLER² AND J. A. BEECH³

ABSTRACT

A description is given of an apparatus suitable for investigations of the oxidation and decomposition reactions of volatile hydrocarbon vapors in a flow system. Most of the reaction products are analyzed quantitatively by gas chromatography in a single-stage process involving a simple column-temperature programming technique. The products of the oxidation of a rich mixture of *n*-pentane and air in an annular reactor of Vycor over a wide temperature range are shown in detailed analysis. The products, as identified by several techniques including time-of-flight mass spectrometry and infrared spectrophotometry, include C_2-C_5 mono-olefins, two di-olefins, C_1-C_4 saturated aldehydes, an unsaturated aldehyde, and 2-methyl tetrahydrofuran in addition to those usually associated with the complete oxidation of *n*-pentane.

INTRODUCTION

Earlier studies in this laboratory of the low-temperature oxidation of *n*-pentane (1, 2) indicated the need for an efficient means of analyzing the complex mixture of products so obtained. It was possible to determine the effect of certain variables on the total concentration of any particular class of components, but this information was insufficient for the determination of a reaction mechanism. The analytical difficulty is largely responsible for the lack of quantitative information concerning the effect of temperature and other variables on the mechanism of the oxidation of hydrocarbons.

One of the first attempts at a detailed analysis was that of Ubbelohde (3), who identified some of the liquid oxidation products of pentane after fractional distillation, using ultraviolet spectroscopy and chemical methods. With the development of liquid partition chromatography and polarography more of the products could be analyzed, as demonstrated by Malmberg and others (4, 5), but the experimental method was complicated and the results were of limited quantitative value.

Detailed analyses of complex mixtures of combustion products can now be effected by using the newly developed gas chromatographic techniques. Thus Yokley and Ferguson (6) were able to investigate qualitatively some of the products of the cool flame combustion of propane; Kyriacos, Menapace, and Boord (7) determined the identity of many of the components of the cool flame combustion products of *n*-hexane, and Hughes, Hurn, and Edwards (8) separated and identified oxygenated hydrocarbons in automotive engine combustion products using a three-stage unit.

Gas chromatography was used in earlier work by the authors to separate liquid oxidation products, in conjunction with Orsat analysis of the normally gaseous products. The liquid products were collected in traps surrounded by dry ice-acetone and ice-water mixtures and the condensates had to be transferred by micrometer syringe to the chromatographic column. This procedure entailed large sources of error in the handling of the samples and volatilization of some of the components. In addition, calculation of selectivities (i.e. moles of product formed/mole of fuel consumed) was tedious because it was necessary to combine the analyses of the two condensates. In addition, the calculations

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²Department of Chemical Engineering, University of Toronto, Toronto, Ontario.

³Present address: Department of Pharmacology, University of Maryland, Maryland, U.S.A.

involved the assumptions of uniformity of the flow rate and the furnace temperature, which were shown to be variable over the long period required for sampling.

The present development of a reproducible sampling method allowed this technique to be extended to a more detailed study of the influence of temperature on the oxidation of an *n*-pentane - air mixture.

APPARATUS

General Description

The apparatus is shown diagrammatically in Fig. 1. The required mixture of carbon-

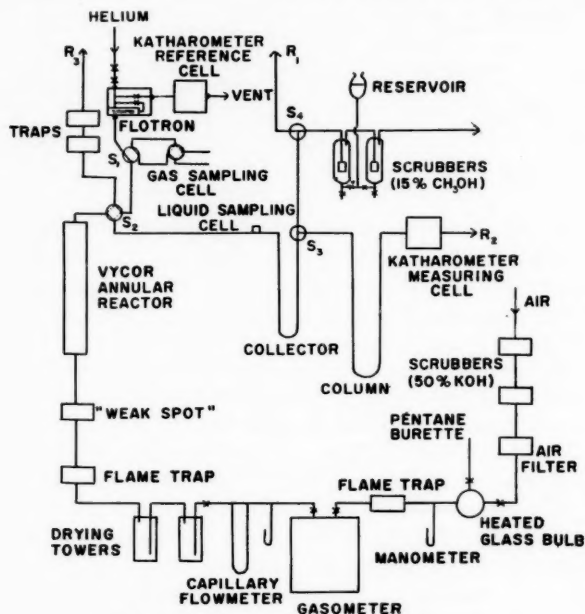


FIG. 1. Schematic diagram of apparatus.

dioxide-free air and *n*-pentane was prepared and stored in the gasometer. From this vessel it was passed at a known rate of flow through the reactor, which, for this study, was constructed of Vycor glass and was annular in form. The reactor dimensions and its positioning in a tubular furnace have already been described (2).

Until steady-state conditions were fully established so that a sample could be taken for analysis, the oxidized mixture was allowed to flow from the reactor through ice-water and dry ice - acetone cooled condenser traps to vent at the rotameter, R_3 .

During this period, the eluent gas (helium) was passed through reducing valves to the Burrell "Flotron". This is a device for maintaining a reproducible volume flow and splitting the eluent stream to allow a small flow through the katharometer reference cell of the modified Burrell K1 Kromotog which was used for the analysis of the condensable oxidation products. The eluent was allowed to bypass the gas sampling cell at S_1 and pass through the collector, the column, and the katharometer measuring cell to vent at the rotameter, R_2 .

Sampling for Chromatographic Analysis

In taking a condensable product sample for chromatographic analysis the flow streams

were redirected so that helium passed through S_2 and the traps to vent at R_2 while the reactor effluent was passed during a measured time interval (usually 5 minutes) through the liquid-air-cooled collector and three-way stopcocks S_3 and S_4 to vent at rotameter R_1 . The collector was a U tube with a side-arm joined to it by a three-way stopcock. It was wound with resistance tape and contained glass wool and a small amount of crushed firebrick to prevent minute crystals of condensate from being blown through it.

To complete the sampling, four-way stopcock S_2 was turned to allow eluent gas to sweep the sample remaining in the lines into the collector. Then stopcock S_3 was turned so that eluent flowed through the column. Finally, the liquid-air bath was removed and the sample in the collector was volatilized into the helium stream proceeding to the column by heating the collector for 4 minutes at about 150° C.

The uncondensed gases emerging at R_1 during the early stages of the above sampling procedure were sampled by microsyringe from the exit line leading to R_1 . This sample was transferred to a homemade chromatographic unit with a Veco thermistor detector cell for analysis on an adsorption column.

The Column Material and Analysis Technique

The separation of the compounds condensed from the reactor effluent was effected on an 8-ft column packed with 25% w/w bis[2-(2-methoxyethoxy)ethyl] ether (MEEE) on 30-60 mesh C-22 firebrick. This substrate was selected as a result of a series of comparison tests using 11 different stationary phases. The operating details for these tests and a comparison of the effectiveness of these substrates for various separations are given in Table I. Subsequently it was observed that the same choice of optimum stationary phase had been made by Yokley and Ferguson (6). Chromatograms of the separations

TABLE I
Comparison of various stationary phases

Stationary phase 25% w/w on 30-60 mesh C-22 firebrick	Maxi- mum usable temp., °C	Ethylene and carbon dioxide separation	<i>cis</i> and <i>trans</i> 2-Pentene separation	Hydro- carbon peaks	Aldehyde peaks	Water peak	Remarks
β,β' -Oxydipropio- nitrile	100	P	P	P	E	F	Unusual order of elution
Acetonyl acetone	20	E	F	E	F	P	Baseline unstable
Dimethyl sulpholane	40	F	P	E	E	E	Unstable at higher temp. otherwise good
Triethanolamine	40	P	P	P	F	P	No peaks beyond acetaldehyde
Acetoacetic ester	40	E	F	F	P	P	Water strongly held
Ethylene glycol monoethyl ether	40	P	P	F	P	P	No peaks beyond pentenes
Triacetin	80	P	P	F	E	E	Good for higher temp. separa- tions
Bis(2-methoxy- ethyl) phthalate	100	P	P	E	E	E	Good for higher temp. separa- tions
Bis[2-(2-methoxy- ethoxy)ethyl] ether	70	E	F	E	E	E	Best stationary phase tested
Dinonyl phthalate	130	P	P	F	F	F	Unusual order of elution
Carbowax 20M	225	P	P	E	E	E	Tested at 60° C; ineffective at 40° C

NOTE: E = excellent, F = fair, P = poor or not observable. Column details: eluent, helium at 50 cc/minute; sample, oxidation products of 54 μ l of *n*-pentane. Column temperature, 40° C.

effected by two of the poorer substrates are shown in Fig. 2. Compounds corresponding to the various peak numbers are listed in Table II. These chromatograms afford yet

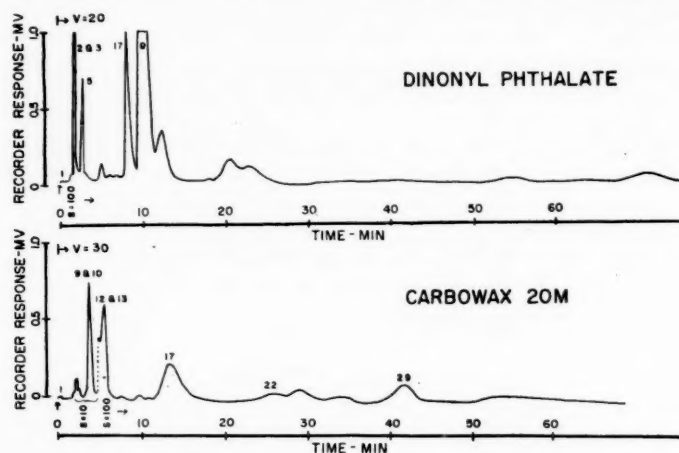


FIG. 2. Comparison of the separations on different substrates.

TABLE II
Identification of products shown in chromatograms

Peak No.	Compound	R.R.T. standards	R.R.T. products	Method of identification		
				M	I	R.R.T.
1	Air	0.00	0.00			x
2	Ethylene	0.06	0.06	x		x
3	Carbon dioxide	0.10	0.10	x		x
4	Unknown		0.18			
5	Propylene	0.18	0.19	x		x
5A	Unknown		0.34			
6	1-Butene	0.46	0.49	x _p		x
7	<i>trans</i> -2-Butene	0.58	0.61	x _p		x
8	<i>cis</i> -2-Butene	0.70	0.72	x _p		x
8A	Unknown		0.95			
9	<i>n</i> -Pentane	1.00	1.00	x	x	x
10	1-Pentene	1.30	1.29	x		x
12	<i>trans</i> -2-Pentene		1.57	x _p		x
13	<i>cis</i> -2-Pentene		1.60	x _p		x
16	Cyclopentane	2.3	2.4	x		x
17	Acetaldehyde	2.7	2.6	x	x	x
18	1,3-Pentadiene		2.9	x _p		
19	1,4-Pentadiene		3.1	x _p		
20, 21	Unknown		3.4			
22	Propionaldehyde	4.3	4.2	x	x	x
23	Acetone	4.7	4.6	x	x	x
24	Acrolein		5.0	x		
25, 26	Methyl alcohol		5.3	x	x	
27	Unknown		5.5			
28	Unknown		5.9			
29	2-Methyl tetrahydrofuran	6.6	6.4	x	x	x
30	<i>n</i> -Butyraldehyde	6.5(?)	7.0	x		x _p
31	Unknown		7.4			
31A	Unknown		8.0			
32, 33	Water	8.8	9.0			x

NOTE: R.R.T. = Relative retention time, *n*-pentane = 1.00 on 25% w/w bis[2-(2-methoxyethoxy)ethyl] ether and 30-60 mesh C-22 firebrick column at 25°C.

M = Mass spectrometry.

I = Infrared spectroscopy.

x = Identified, x_p = tentatively identified.

another example of the remarkable versatility of the gas-liquid chromatographic technique. Thus, the order of elution of the polar compound, acetaldehyde (peak 17), relative to the non-polar *n*-pentane (peak 9), can be radically altered, as shown, by suitable choice of stationary phase polarity.

The following very simple but quite effective system of column-temperature programming was used to obtain a reasonably efficient separation of the condensed sample in a single operation. The column temperature at the beginning and for the first 10 minutes of each analysis was 25° C. At the end of this period an electric current at a potential of 30 volts was passed through the resistance wire wound on the column. The rate of increase of temperature was such that a temperature of 60° C was attained in another 15 minutes. A fixed eluent flow rate of 100 ml per minute (25° C and 760 mm Hg), as measured at the downstream end of the chromatograph, was always maintained by the "Flotron". Hence there was little or no change in the base line due to the temperature change.

With the MEEE substrate a low initial temperature was ideal for the separation of carbon dioxide and the lower olefins. On the other hand, the gradually increasing temperatures in the following period prevented excessive peak broadening of the higher boiling components without seriously impairing their separation. The temperature finally attained allowed the analyses to be completed in less than 1 hour. A representative chromatogram obtained in this manner from a 5-minute sample of the reactor effluent taken when the maximum wall temperature was 509° C is given in Fig. 3. The excellent

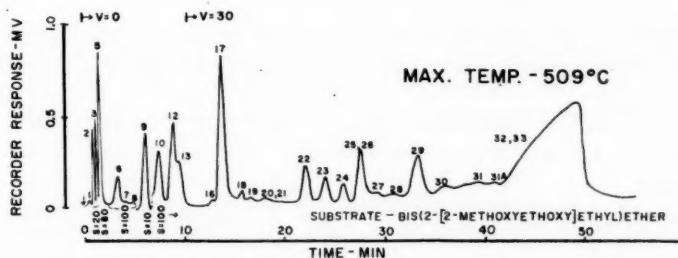


FIG. 3. Representative oxidation product chromatogram.

separation of most of the constituents and the stability of the base line despite the relatively large change in column temperature are readily apparent.

A further temperature increase to 90° C would have permitted the analysis of part of the organic acid content of the sample. However, a noticeable "bleeding" of the substrate occurs at this temperature. Hence, the analysis for the acid content was performed on a separate sample by a titration method.

The uncondensed gases were separated on a 15-ft column of 30-60 mesh 5A Linde molecular sieves. This material was dried for 6 hours in a nitrogen stream at a temperature of 300° C prior to packing. Hydrogen, oxygen, nitrogen, methane, and carbon monoxide were readily separated and all but the hydrogen were quantitatively determined on this column at a temperature of 100° C with helium flowing at 50 ml per minute. With this eluent, the sensitivity for hydrogen was about 1/20th of that for the other gases due to the similarity of its thermal conductivity to that of helium. Hence quantitative results for this gas were not obtained unless its concentration exceeded about 1% by volume of the uncondensables.

Formaldehyde Analysis

Initially, it was hoped to measure formaldehyde by gas chromatography. However, a number of experiments showed that polymerization of formaldehyde at low temperatures would require the use of a column temperature exceeding 100° C and controlled within fine limits. At these elevated temperatures a formaldehyde peak was observed. However, other oxidation products which could not be resolved interfered and a quantitative determination could not be made. In addition the substrate "bleeding" mentioned earlier became appreciable at temperatures above 100° C and the useful life of the column was thereby excessively reduced. Work on a gas chromatographic separation of formaldehyde is continuing.

The polarographic methods for formaldehyde could not be applied because of the mixture complexity and especially because of the presence of acrolein, which interferes. Hence, a chemical method of analysis was indicated. Since a large number of analyses was projected the specific reaction with chromotropic acid as recommended by West and Sen (9) was adopted rather than the precipitation and separation of derivatives.

The sample was collected prior to the one for gas chromatographic analysis by a precisely similar technique. This was transferred to and absorbed in scrubbers containing 15% methyl alcohol. An aliquot of this solution was treated with chromotropic acid in sulphuric acid solution. After the mixture was heated in a boiling water bath for 5 minutes to develop the color, the color maximum at 560 m μ was read and compared with that of a similarly treated standard formaldehyde solution.

Acid Analysis

The sampling technique was modified by (a) condensing the sample in a dry ice-acetone cooled collector and (b) absorbing this sample in a scrubber containing 0.01 *N* sodium hydroxide. An aliquot of this solution was backtitrated with 0.01 *N* hydrochloric acid solution to the phenolphthalein end point. The results were calculated as formic acid.

Peroxide Analysis

Liquid air was again used for condensation and the sample was run into a scrubber containing isopropyl alcohol. An aliquot of this solution was analyzed by iodometric titration. Since the peroxide content of the effluent in the conditions of these experiments proved to be negligible, the more sensitive test of Widmaier and Mauss (10) was also applied. Again, results indicated the absence of peroxides.

PRODUCT IDENTIFICATION

The qualitative analysis of the oxidation products was effected using several techniques and is still not quite complete. The Bendix time-of-flight mass spectrometer, applied as described by Gohlke (11), successfully identified several compounds. At 100 intervals during the running of the chromatograms the column effluent was leaked into the mass spectrometer and a full mass spectrum of the compound was obtained by a very sensitive amplification and rapid-scan method. A representative spectrum which was identified as that due to 2-methyl tetrahydrofuran is shown in Fig. 4.

Our experience in the interpretation of spectra from the time-of-flight mass spectrometer leads to the following conclusions:

(a) Several compounds may be scanned at the same time if the chromatographic column does not have sufficient resolving power. However, by comparing scans taken at the beginning and end of a peak elution this can be detected more easily than by conventional mass spectrometer.

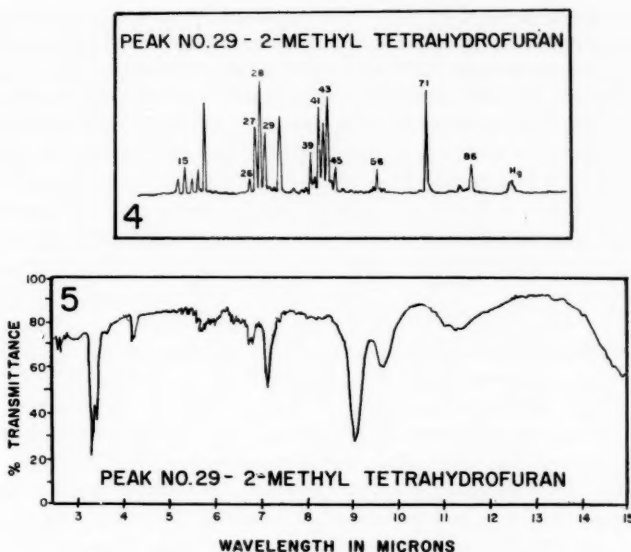


FIG. 4. Representative time-of-flight mass spectrum.

FIG. 5. Representative micro-gas-cell infrared spectrum.

(b) The accelerating chamber or the spectrometer lead-in is not completely swept between samples. As a result, there is a doubt as to whether any given peak is retained from a previous scan.

(c) With the mass scale used in our analyses, the numerical value of mass numbers greater than 80 was uncertain. We have, however, been informed that wider mass scales are now available.

(d) The background peaks gradually change in height when a number of scans is taken. There is therefore no way of knowing which contribution of a given mass is due to background and which to the component. This fault is also to be found, to a lesser extent, with conventional mass spectrometers.

Despite the above comments, the time-of-flight mass spectrometer has great potentialities for use in this field. The identity of most of the peaks analyzed by this means was confirmed by trapping the compound as it left the column and analyzing it by conventional mass spectrometer. For small peaks adjacent to large ones, however, the time-of-flight machine had a decided advantage.

In addition to the above analyses, the identity of seven of the peaks was confirmed by using a combination of gas chromatography and infrared spectrophotometry. Samples of the effluent from the chromatographic column were passed directly into a 600-mm path-length infrared micro-gas-cell designed by White (12). These were analyzed in a Beckman IR 4 infrared spectrophotometer equipped with a micro-optical system.

The spectrum of a representative reaction product peak, 2-methyl tetrahydrofuran, is shown in Fig. 5. It should be emphasized that the procedure described above was purposely adopted for convenience of sampling, i.e. to eliminate the troublesome sample freeze-out and transfer steps usually required. To do this, optimum spectrophotometric operating conditions were abandoned. Thus, for example, sample pressure was one atmosphere (mostly helium) rather than 50–100 mm Hg as usually recommended.

The infrared spectra thus obtained were correspondingly poorer than they might have been. Better resolution is obtained by trapping the samples in a liquid-air-cooled vessel, which may subsequently be evacuated while cool to remove helium and from which the sample may be flashed into the evacuated micro-gas-cell to the optimum pressure.

Further confirmation of the identity of any suspected component was obtained, whenever a sample of the pure compound was available, by comparison of their retention times relative to that of *n*-pentane. The compounds listed in Table II were identified by one or more of the above techniques. The relative retention times (*n*-pentane = 1) for these compounds are included in Table II. These values are the averages of from 5 to 15 determinations each, with deviations, generally, of less than $\pm 5\%$.

QUANTITATIVE EVALUATION OF RESULTS

To convert component peak areas to component concentrations, known volumes of pure compounds were analyzed under conditions similar to those used for the oxidation product mixture and calibration factors were then calculated. With eluent gas flowing through the column and the collector in a liquid-air bath, the standards were injected on to the heated connecting tube through a silicone seal in the liquid sampling cell and the eluent carried them into the collector where they were condensed. They were then transferred to the column by the technique already described. When the actual compound to be measured was not available in the pure state a similar type of compound was used as a standard. Where the peak was not positively identified the figures used for molecular weight and density in the calculation of selectivity were estimated on the basis of the suspected values. The concentrations were calculated by weight ratio. Generally areas were estimated as the product of peak height and peak width at half height. Where the base line undulated, the areas were measured by planimeter. For the water peak a piece of paper equal to the peak in area was weighed and for the earlier peaks, peak height was more convenient to measure than area.

RESULTS AND DISCUSSION

The state of the surface of the reactor is known to affect the initial rate at which oxidation occurs. The material of the reactor, together with the interrelated shape, mixture residence time, and flow configuration also affects the course of the reaction. When the reactor was first used it was found to give erratic results. Stability of the surface was rapidly obtained, however, when a little nitric acid was introduced at about 500° C and the temperature was slowly raised to 1000° C. After cooling the reactor to 500° C, a stream of helium was passed through until no chromatographic peak due to the nitric acid was obtained from a sample of the effluent.

On establishing that a fairly stable and reproducible surface could be prepared in this way, at least for the reaction of rich mixtures of pentane and air, a preliminary program was outlined for demonstrating the effectiveness of the gas chromatographic method and for obtaining new information regarding the effect of temperature on the product distribution from the reaction of one particular mixture of *n*-pentane and air. This program consisted of a series of runs at certain temperatures between 375 and 800° C with a 1.3 stoichiometric *n*-pentane - air mixture supplied to the reactor at the rate of 100 ml/minute as measured at 25° C and 1 atmosphere pressure. Product analyses were carried out on samples of the effluent from each run as outlined previously using both gas chromatographic and chemical methods.

A representative chromatogram of the oxidation products of *n*-pentane obtained from

a run at a maximum reactor wall temperature of 509° C has been given in Fig. 3. By reference to Table II, which gives the key to the peak numbers, an idea of the mixture complexity and of the particular value of this method of analysis may readily be obtained. The results of calculations made from a series of such chromatograms in conjunction with those obtained from the chemical analyses are presented in Table III and Figs. 6-9.

TABLE III
Carbon balances
(carbon selectivity, %)

Temperature, °C	450	500	550	600	650	700	750	800
Oxides of carbon	22.5	15.4	12.0	9.8	8.7	16.0	55.2	71.6
Aldehydes and ketones	24.2	24.9	23.4	20.1	15.8	9.7	2.6	0.1
Methyl alcohol	8.4	5.4	2.2	0.4	—	—	—	—
2-Methyl tetrahydrofuran	17.8	20.0	18.6	14.2	9.0	3.5	—	—
Methane	—	—	—	—	1.2	4.0	4.9	4.5
Acids	4.6	4.4	2.6	0.3	—	—	—	—
Olefins	15.4	21.2	28.2	35.5	43.2	33.2	13.3	9.1
Deficiency	7.1	8.7	13.0	19.7	22.1	33.6	24.0	14.7

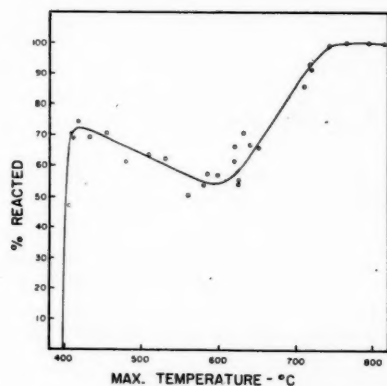


FIG. 6. The effect of temperature on the percentage of *n*-pentane reacted.

In Fig. 6 the percentage of pentane reacted is plotted against maximum reactor wall temperature. The curve for *n*-pentane reacted rises sharply to a maximum at 410° C and then falls off slowly as the temperature increases to 625° C demonstrating again the now familiar negative temperature coefficient of the reaction in these conditions. From this point the percentage of pentane reacted rises sharply to 100%. The second sharp rise in the curve occurs when the mechanism of the over-all process changes so that carbon monoxide, carbon dioxide, and water become the major oxidation products.

The variations in product distribution with reactor temperature are indicated in Figs. 7-9. Several facets of the results deserve comment.

1. The absence of peroxides is significant in view of the proved sensitivity of the methods of detection employed. However, on the basis of former studies with a reactor of high surface-to-volume ratio (2), this result was not unexpected.

2. The surprisingly high concentration of 2-methyl tetrahydrofuran in the products, which accounts for as much as 20% of the carbon content of the *n*-pentane reacted, Table III, should be noted. The conditions of high surface-to-volume ratio and nitric acid pretreatment of the surface seem to favor the formation of this product.

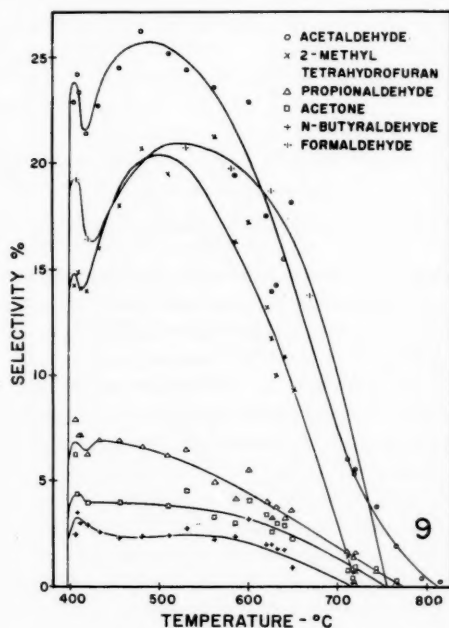
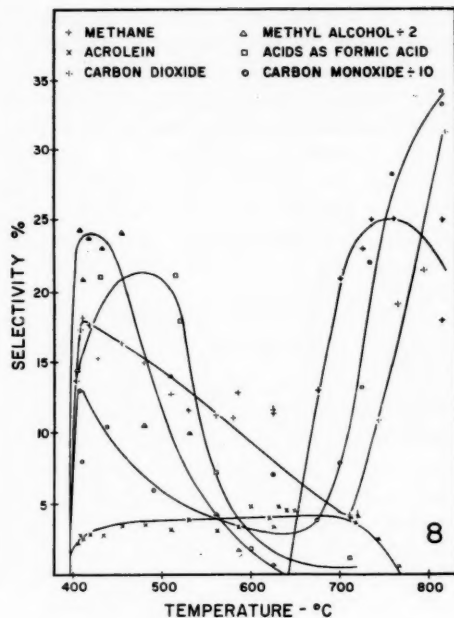
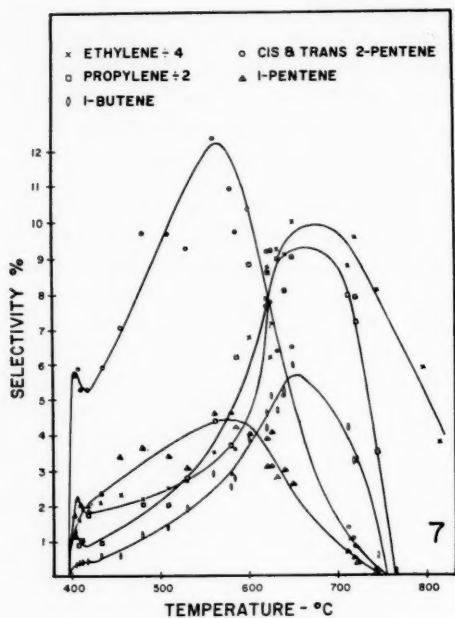


FIG. 7. The effect of reactor wall temperature on olefin selectivity.
 FIG. 8. The effect of reactor wall temperature on product selectivity.
 FIG. 9. The effect of reactor wall temperature on product selectivity.

3. A small but quite distinct dip in the product selectivities (Figs. 7 and 9) for the olefins and oxygenated compounds other than the acids, methanol, and oxides of carbon occurs at about 420° C. This is followed by a rapid increase in product concentration to a maximum and finally by a more gradual decrease.

4. A two-stage reaction mechanism, at least, is indicated. Methane is a product of the high-temperature reaction. Its formation is not evident below about 650° C (Fig. 8). On the other hand, the rate of formation of methanol and organic acids becomes negligible at this temperature. It is interesting that the high methane concentration in the high-temperature region is not accompanied by a correspondingly high hydrogen content (the hydrogen concentration was not detectable). This is further confirmation of the view that the lower olefins are formed via an oxidation mechanism and not by simple pyrolysis of the hydrocarbon in this temperature range.

5. The rate of formation of the simple olefins, ethylene, propylene, and butylene, becomes a maximum at about 700° C and the mechanism at higher temperatures appears to involve the further oxidation of these olefins. Ethylene is the most stable in this regard. The higher olefins attain their maximum concentrations at lower temperatures (550°–600°). When the concentration of the simpler olefins has reached a maximum that of the higher olefins has become negligible.

6. Epoxides, such as ethylene and propylene oxides, which were postulated by Boord (13) and observed by Kyriacos, Menapace, and Boord (7), were not found in the present study but may have escaped detection since they come off near the large acetaldehyde peak.

7. The relatively constant acrolein concentration (Fig. 8) over the wide range of temperature between 400 and 700° C is remarkable. An explanation for this observation is not available at this time.

8. The relative preponderance of carbon monoxide over carbon dioxide in the products (Fig. 8) is consistent with the results expected from the oxidation of a rich mixture.

9. Carbon balances on the identified products of the reaction for selected temperatures from the product selectivity-temperature graphs are given in Table III. A useful and rapid means of obtaining these carbon balances has been employed here. This is the concept of a carbon selectivity of a particular product, which may be defined as the product of component percentage selectivity and the ratio of the number of carbon atoms per mole of component and reactant respectively. Considering the omission from this tabulation of the carbon in the minor and the unidentified components and in those compounds less volatile than water, these balances indicate that this method of analysis can be used to provide the detailed information required to study the kinetics and mechanism of complex reactions.

CONCLUSION

1. The purpose of this preliminary work was to develop an integrated apparatus for the investigation of an oxidation or decomposition reaction with the principal aid of the gas chromatographic technique. In this respect a method of sampling has been described which will obviate many of the difficulties associated with the transfer of gaseous or liquid samples from the reactor to the gas chromatographic apparatus and will also allow samples to be taken for the more usual chemical or physical methods of analysis. Most of the condensable products may be analyzed in a single-stage process by a simple column-temperature programming technique.

2. The use of several qualitative microanalytical methods including time-of-flight

mass spectrometry and infrared spectrophotometry for identifying the products separated by the gas chromatographic method has been described and critically evaluated.

3. Although a mechanism for the reaction studied here will not be presented until further studies involving the effects on product distribution of varying the mixture strength, residence time, and condition of the surfaces have been completed, some of the interesting features of the results have been discussed. Thus, a method of obtaining a reproducible surface has been described, variations in product distribution with temperature have been noted, and the presence of certain suspected and some unsuspected compounds in the reaction product mixture has been confirmed or determined.

ACKNOWLEDGMENTS

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THE STRUCTURE OF MONOBROMINATED ETHYL INDOLE-3-CARBOXYLATE AND THE PREPARATION OF 7-BROMOINDOLE¹

B. E. LEGGETTER AND R. K. BROWN

ABSTRACT

The compound reported by Majima and Kotake as ethyl 6-bromoindole-3-carboxylate, obtained from the monobromination of ethyl indole-3-carboxylate, when saponified, decarboxylated, and the product repeatedly crystallized from alcohol, actually gave a nearly equimolar mixture of 5- and 6-bromoindoles of constant melting point, 74–75°. 7-Bromoindole has been synthesized by two unambiguous routes.

INTRODUCTION

Majima and Kotake have reported the preparation of ethyl 6-bromoindole-3-carboxylate via bromination in acetic acid of ethyl indole-3-carboxylate (1). Their proof of structure rested upon the observation that dibromination, in acetic acid, of ethyl indole-3-carboxylate actually gave ethyl 5,6-dibromoindole-3-carboxylate, a fact established by the isolation of 5,6-dibromoisatin and 4,5-dibromo-2-amino-benzoic acid. Since the *monobrominated* compound gave a monobromoisatin quite different from the authentic 5-bromoisatin previously prepared by Borsche and Jacobs (2) and in view of the established structure of the dibrominated product, it was concluded that monobromination of ethyl indole-3-carboxylate had occurred at position 6. The discrepancy between the melting point of their "6-bromoisatin" (256–258°) and that of Ettinger and Friedlander's 6-bromoisatin (m.p. 263–264°) (3) was attributed to contamination of their monobromoisatin with some 5,6-dibromoisatin.

The monobrominated ethyl indole-3-carboxylate of Majima and Kotake, saponified and decarboxylated in this laboratory, gave a monobromoindole melting at 74–75° which, according to the assignment of the Japanese authors, should be 6-bromoindole. A recently reported unambiguous preparation of 6-bromoindole (4) melting at 94° casts doubt upon Majima and Kotake's structural assignment. This was further intensified by observation in this laboratory of a marked depression of the melting point of a mixture of these two bromoindoles. That the compound melting at 74–75° is neither 4- nor 5-bromoindoles is shown by comparison of their physical constants. Authentic 4-bromoindole (4) is a liquid which we found to boil at 89–92°/0.25 mm and which has a refractive index of 1.6566 at 21°, while 5-bromoindole melts at 88.5–89° (5). Furthermore, the infrared spectra of the 4-, 5-, and 6-bromoindoles failed to correspond with that obtained for the questionable bromoindole.

Since the possibility existed that the as yet unknown 7-bromoindole might actually be the compound synthesized by Majima and Kotake, its preparation was undertaken. The precursor, 7-bromoindole-2-carboxylic acid, was made by two unambiguous routes. The first method entailed the preparation of ethyl pyruvate 2-bromophenylhydrazone, which was then subjected to Fischer ring closure with polyphosphoric acid. The second method involved the conversion of 3-carboxy-2-nitrotoluene (6) to 3-bromo-2-nitrotoluene by the Hunsdiecker reaction (7). A Reissert condensation of 3-bromo-2-nitrotoluene with ethyl oxalate (5), affording optimum yields only after prolonged reaction between the ester and the nitrotoluene at room temperature, gave ethyl 3-bromo-2-nitrophenylpyruvate. This was converted to 7-bromoindole-2-carboxylic acid by the usual reductive ring closure.

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Contribution from the Department of Chemistry, University of Alberta, Edmonton, Alberta.

The 7-bromoindole-2-carboxylic acid gave unsatisfactory decarboxylation by the usual procedures (4, 5, 8). However, a modified version of one method (8, 9), in which the acid was refluxed in synthetic quinoline for 48 hours while small amounts of copper chromite (10) were added at frequent intervals, gave a 48% yield of 7-bromoindole. This synthesis now makes available the last of the isomeric benzene ring-monobrominated indoles.

The infrared spectrum and melting point (42–43°) of 7-bromoindole showed conclusively that it was not the "6-bromoindole" derived from the "ethyl 6-bromoindole-3-carboxylate" of Majima and Kotake.

Comparison of the infrared spectra of 5- and 6-bromoindoles suggested that the unknown substance might be a mixture of the two. Accordingly, when samples containing various proportions of the two isomeric bromoindoles were prepared, it was found that a mixture of 45% of 5-bromoindole and 55% of 6-bromoindole gave a spectrum identical in every respect with that of the unknown. The bands at 1308 cm^{-1} for the 5-isomer and at 1329 cm^{-1} for the 6-isomer have nearly equal intensities and can be used as a reasonably good method for estimation of the relative amounts of these two isomers in a mixture. The two isomers can be clearly distinguished by the absorption bands shown in the following table.

Compound		Absorption bands at: (cm^{-1})						
6-Bromoindole	665 (w)	800 (s)	840 (m)	852 (w)	864 (w)	1305 (w)	1329 (s)	
5-Bromoindole	664 (s)	788 (s)	Nil	Nil	864 (s)	1308 (s)	1329 (w)	

NOTE: w, m, and s are respectively weak, medium, and strong.

Neither the melting point of this mixture (74–75°) nor its composition could be altered by repeated crystallization. Similar constant-melting mixtures of isomeric compounds have been recorded in the literature, a specific example being the isomeric 5- and 7-nitro-1,2,3,4-tetrahydrocarbazoles, a mixture of which crystallizes in equimolecular proportion from a variety of solvents to form a substance of constant composition and melting point (11). However, unlike the case of the tetrahydrocarbazoles, chromatography does not readily separate the 5-bromoindole from the 6-bromoindole. Since a single chromatographic operation using an alumina column did in fact achieve a partial separation, as shown by the change in the infrared spectra of the fractions, it is no doubt possible by repeated and careful chromatography to separate them completely.

We have repeated the bromination of ethyl indole-3-carboxylate as described in the literature and obtained the same results (1). Several crystallizations of the ethyl bromoindole-3-carboxylate from aqueous alcohol failed to alter the melting point of 134–137°. A sample of this substance, passed through a column of activated alumina, gave very little separation. Chromatography of the fractions obtained from this first attempt at separation also gave unsatisfactory results. However, since the melting points of the various fractions did in fact differ somewhat both in value and in range from each other it was assumed that, as for the case of the 5- and 6-bromoindoles, a separation could be achieved by painstaking care. It is to be noted that crystallization of each of these various fractions from diluted alcohol again gave the material of constant melting point of 134–137°.

Hydrolysis of the ester according to the literature (1) gave an acid which upon several crystallizations from 95% alcohol melted at 212°, a fact which had already been recorded (1). No attempt was made to separate this substance into its isomers. Our decarboxylation

of this compound in quinoline at 140° afforded a compound whose analysis, following several crystallizations from alcohol, agreed with that of a monobromoindole and is now known to be a nearly equimolar mixture of 5- and 6-bromoindoles (m.p. 74–75°).

This work indicates that not only do 5-bromoindole and 6-bromoindole form a constant-melting mixture, but that their precursors, 5- and 6-bromoindole-3-carboxylic acid and the ethyl ester, do likewise. Whether the precursors are nearly equimolar mixtures is uncertain. However, if that is so, then ease of bromination of ethyl indole-3-carboxylate is approximately equal for the 5 and the 6 positions.

EXPERIMENTAL

All melting points are uncorrected. The 4-bromoindole (4), 5-bromoindole (5), and 6-bromoindole (4) were prepared according to the published procedures.

3-Bromo-2-nitrotoluene

Bromine (24 g, 0.15 mole) was added slowly to a stirred suspension of 41.5 g (0.144 mole) of silver salt of 3-methyl-2-nitrobenzoic acid in anhydrous carbon tetrachloride (350 ml) at 25°. Following the addition, the mixture was heated to reflux for 3 hours, during which time carbon dioxide was evolved. The cooled solution was freed from silver salts and the filtrate washed first with aqueous sodium bisulphite, then with aqueous sodium bicarbonate, and finally with water, and then dried over anhydrous magnesium sulphate. Removal of the sulphate and ether afforded a brown oil which, when steam distilled, yielded 18.0 g of 3-bromo-2-nitrotoluene (58%) melting at 27°, lit. m.p. 27° (12).

Potassium Enolate of Ethyl 3-Bromo-2-nitrophenylpyruvate

Potassium (2.3 g, 0.059 mole) was dissolved in anhydrous ethanol (20 ml). To this solution, diluted with 100 ml of dry ether, was added 8.7 g (0.059 mole) of diethyloxalate and the mixture was then stirred gently for 15 minutes. The addition of an ether solution of 11.0 g (0.05 mole) of 3-bromo-2-nitrotoluene produced a deep orange solution which, left at 25° for 7 days, slowly deposited the potassium salt as an orange precipitate. The solid was collected, washed thoroughly with anhydrous ether, and air-dried, yielding 12.1 g (67%) of product.

Ethyl 3-Bromo-2-nitrophenylpyruvate

When a small portion of the above potassium salt was dissolved in water, cooled to 0°, and acidified carefully with 6 *N* hydrochloric acid, a bright yellow solid precipitated. Crystallization from ethanol gave a melting point of 114–115°, which further crystallization failed to alter. Calc. for $C_{11}H_{10}BrNO_3$: C, 41.84; H, 3.17; N, 4.43. Found: C, 41.83; H, 3.19; N, 4.24.

7-Bromoindole-2-carboxylic Acid

A solution of the potassium enolate of ethyl 3-bromo-2-nitrophenylpyruvate (3.0 g, 0.009 mole) in warm 4 *N* ammonium hydroxide (100 ml) was slowly added, with stirring, to a boiling suspension of ferrous hydroxide prepared by the addition of ammonium hydroxide (6 ml, $d = 0.880$) to a boiling solution of ferrous sulphate heptahydrate (14.0 g, 0.05 mole) in 100 ml of water. The resulting reduction mixture was maintained at 90° for 30 minutes and then filtered from the ferric oxide sludge. The sludge was extracted three times with boiling 2 *N* ammonium hydroxide and the combined filtrate and extracts cooled to 25° and acidified with 6 *N* hydrochloric acid. The solid, collected by suction filtration, when crystallized once from aqueous ethanol gave 1.2 g (60%) of 7-bromoindole-2-carboxylic acid melting at 236–239°. Repeated crystallization gave an

analytical sample of melting point 242–244°. Calc. for $C_9H_6BrNO_2$: C, 45.00; H, 2.50; N, 5.83. Found: C, 45.20; H, 2.58; N, 5.99.

7-Bromoindole

A solution of 7-bromoindole-2-carboxylic acid (2.9 g) in synthetic quinoline (20 ml) was refluxed for 48 hours, during which time small amounts of copper chromite (10) catalyst were added at frequent intervals. The cooled reaction mixture was poured into 350 ml of 1 *N* hydrochloric acid and the resulting solution extracted thrice with 150-ml portions of ether. The combined ether extracts, washed twice with 1 *N* hydrochloric acid, once with water, twice with 1 *N* ammonium hydroxide, and then with water, were dried over anhydrous magnesium sulphate. Removal of the ether yielded a yellow oil which was purified by chromatography on an alumina column, using *n*-pentane as eluant, giving 1.13 g (48%) of colorless crystals melting at 42–43°. Calc. for C_8H_6BrN : C, 48.98; H, 3.06; N, 7.14; Br, 40.81. Found: C, 49.08; H, 3.09; N, 7.13; Br, 40.42.

Ethyl Pyruvate 2-Bromophenylhydrazone

A solution containing ethyl pyruvate (15.3 g, 0.13 mole) (13), 2-bromophenylhydrazine (24.1 g, 0.13 mole) (14), and ethanol (50 ml) was refluxed for 1 hour, cooled, and poured into cold water. The precipitated yellow solid, when air-dried and crystallized for ethanol, gave 33.1 g (91%) of product melting at 44–46°. Calc. for $C_{11}H_{13}BrN_2O_2$: C, 46.32; H, 4.56; N, 9.86. Found: C, 46.36; H, 4.63; N, 9.78.

Ethyl 7-Bromoindole-2-carboxylate

A mixture of ethyl pyruvate 2-bromophenylhydrazone (33.1 g) and polyphosphoric acid* (40 g) was slowly heated. When the temperature of the mixture reached 70° a spontaneous exothermic reaction occurred raising the temperature to 150°. The reactants were kept at this temperature for 10 minutes, then cooled and poured into cold water. The ether extracts of this solution when dried with anhydrous magnesium sulphate gave a brown oil which solidified. Crystallization from ethanol yielded 14.3 g (46%) of product, m.p. 85–86°. Calc. for $C_{11}H_{10}BrNO_2$: C, 49.25; H, 3.73; N, 5.22. Found: C, 49.01; H, 3.74; N, 5.17.

When 14.3 g of ethyl 7-bromoindole-2-carboxylate was dissolved in a mixture of ethanol (200 ml) and 2.5 *N* aqueous sodium hydroxide solution (70 ml), refluxed for 2 hours, poured into cold water (1000 ml), and then acidified with 6 *N* hydrochloric acid, a solid deposited which after crystallization from ethanol afforded 7.1 g (55.5%) of product melting at 237–239°. This was found to be identical with the 7-bromoindole-2-carboxylic acid prepared above.

Decarboxylation of the Mixture of 5- and 6-Bromoindole-3-carboxylic Acids

Twelve grams of the monobromoindole-3-carboxylic acid mixture (m.p. 212°) (1) in 25 ml of quinoline was heated to 140° whereupon vigorous evolution of carbon dioxide ensued. The temperature was maintained at 140° for 2.5 hours, after which time no further evolution of carbon dioxide occurred. The reaction mixture was then poured into 300 ml of 1 *N* hydrochloric acid and a dark oil separated. The oil solidified and was collected, washed with 1 *N* hydrochloric acid, and then with water. Crystallization from aqueous alcohol yielded a product melting at 74–75°, which repeated crystallization from aqueous alcohol, skellysolve, or heptane failed to alter. Yield, 4.3 g (46%). Calc. for C_8H_6NBr : C, 49.0; H, 3.1. Found: C, 48.7; H, 2.9.

*Commercially available from Victor Chemical Works, Chicago, Illinois.

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SYNTHESES OF POLYURETHANES FROM HYDROXY-TERMINATED POLYESTERS¹

PAUL E. GAGNON, JEAN-L. BOIVIN,² AND GEORGE W. HOUSE³

ABSTRACT

Hydroxy-terminated polyesters were synthesized by treating diols with the diethyl esters of dicarboxylic acids. Ethylene, diethylene, and triethylene glycols, four polyoxyethylene glycols ranging in molecular weight from 200 to 600, 1,2-propanediol, dipropylene glycol, five polyoxypropylene glycols ranging in molecular weight from 150 to 2025, 1,3-propanediol, 1,3-butanediol, 1,4-butanediol, 2,3-butanediol, 1,5-pentanediol, 2,2'-(methylimino)diethanol, 2,2'-(ethylimino)diethanol, 2,2'-(butylimino)diethanol, and 2,2'-thiodiethanol were condensed with diethyl succinate in the absence and presence of a catalyst, and with diethyl cyanomalonate, cyanosuccinate, and α -cyanoglutarate.

Polyurethanes were obtained from the various polyesters prepared by treatment with different quantities of 2,4-tolylene diisocyanate. In general, non-elastomeric products were obtained from polyesters of monomeric glycols, while elastomeric polyurethanes with the lowest brittle points were formed from polyoxyethylene glycol 400 and 600, and polyoxypropylene glycol 750, 1025, and 2025 polyesters. Also the succinate polyurethanes, which did not contain nitrile groups, had the greatest tendency to be elastomeric and had the lowest brittle points. For the nitrile containing polyurethanes, the cyanomalonates had the lowest tendency to be elastomeric and had the highest brittle points. The cyanosuccinate and α -cyanoglutarates had about the same properties.

INTRODUCTION

Polyesters constitute an important class of synthetic polymers employed as textiles, resins, and intermediates for the preparation of polyurethanes. They can be prepared by the reactions commonly used to obtain simple esters. Hydroxy-terminated polyesters are produced by heating diols in excess with dibasic acids or esters and by continuing the heating under vacuum to yield high molecular weight polymers (1).

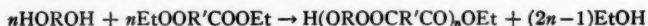
Polyurethanes are made by reacting polyhydroxylated compounds or polyesters with diisocyanates. They have found extensive use as rubber substitutes (2, 3, 4, 5), foams (6), coatings (7), and adhesives (8).

In the present investigation, the main object was the synthesis of polyesters and polyurethanes, some containing nitrile groups, and the comparison of their properties.

RESULTS AND DISCUSSION

Polyesters

Polyesters were prepared by the transesterification of different diols with diethyl succinate, cyanomalonate, cyanosuccinate, and α -cyanoglutarate.



It was observed that the general order of reactivity of diols was thus: (a) the basic and therefore self-catalyzed N-substituted iminodiethanols, (b) the other monomeric glycols bearing two primary hydroxyl groups, (c) monomeric glycols bearing one or two secondary hydroxyl groups, (d) polymeric glycols bearing solely primary hydroxyl groups, and (e)

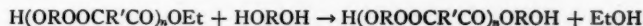
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²Contribution from the Department of Chemistry, Laval University, Quebec, Que. This paper constitutes part of a thesis submitted to the Graduate School, Laval University, in partial fulfillment of the requirements for the degree of Doctor of Science.

³Canadian Armament Research and Development Establishment, Valcartier, Que.

⁴Graduate student, holder of National Research Council of Canada Studentships in 1957-60.

polymeric glycols bearing solely secondary hydroxyl groups. To terminate the chains by hydroxyl groups, an excess of glycol was added to the reaction mixture and heating continued.



Then the reaction was driven towards completion and excess glycol was removed under vacuum.

Succinates

The reaction between diethyl succinate and the glycols in the absence of a catalyst proceeded only quite slowly and in most cases ethanol distilled at temperatures ranging from 155 to 215° C, and prolonged reaction times were necessary.

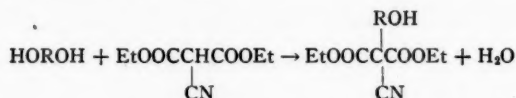
The molecular weights of the products, measured by hydroxyl end-group analysis, varied from 500 to 3540 but were for the most part between 800 and 2000. The values found for the polyesters of polyoxyethylene glycol 600 and polyoxypropylene glycols 425, 750, 1025, and 2025 were higher than the true molecular weight values because no excess glycol had been employed to assure the termination of polyester chains by hydroxyl groups. Furthermore, the values found for the polyesters of polyoxypropylene glycols 1025 and 2025 were certainly not high as compared to the molecular weights of the glycols themselves, indicating that very little reaction had taken place.

In order to investigate the effect of an ester interchange catalyst on the rate of the polyesterification reaction and on the molecular weight of the product, the syntheses of the succinate polyesters were repeated in the presence of a sodium catalyst. It was observed that ethanol began to form at reaction temperatures well below those of the corresponding preparations carried out without catalyst, 70 to 90 degrees lower in most cases. Distillation was also much more rapid and complete with catalyst than without. In the case of 1,2-propanediol, for instance, without catalyst 25% of the theoretical amount of ethanol had collected after 114 hours of reaction time at 190° C, whereas with a catalyst 82% of the theoretical amount of ethanol had collected after 17 hours at the same temperature. The molecular weights of the products varied between 670 and 3620, although most lay in the region 1000 to 2000. In general, these molecular weights were higher than those of the corresponding products formed without catalyst. The viscosities of polyesters, which were of roughly the same molecular weight when prepared by either method, were higher for products prepared using catalyst than for those prepared without.

Cyanomalonates

Diethyl cyanomalonate was obtained from the reaction of the sodium derivative of ethyl cyanoacetate and ethyl chloroformate (9). The transesterification between diethyl cyanomalonate and the glycols proceeded quite rapidly, ethanol beginning to distill at reaction temperatures about the same as those in the syntheses of the corresponding succinate polyesters prepared with catalyst, and much lower than those in the syntheses of succinate polyesters prepared without catalyst. In addition, ethanol was collected more rapidly and more completely than in the syntheses of the corresponding succinate polyesters without catalyst. However, the molecular weights of the polyesters, based on hydroxyl end-group analysis and the assumption of two hydroxyl groups per molecule, were very low, below 500 in most cases. Thus it would appear that diethyl cyanomalonate, although much more reactive than diethyl succinate, gave polyesters of lower molecular weight.

The high reactivity of diethyl cyanomalonate ($pK_a = 4.76$ at 25°C) was explained by its acidity, which catalyzed the transesterification reaction with glycols. Furthermore, because of the acidity the central carbon atom of the ester was assumed to be alkylated by a glycol, with the formation of water.



The resulting alkylated molecule, which possessed two ester groups and one hydroxyl group, would then undergo a series of transesterifications and alkylations. In the presence of excess glycol, polymeric cross-linked molecules containing many hydroxyl groups could build up.

The apparently low molecular weight of the cyanomalonate polyesters could thus be explained by the assumption that each molecule contained several rather than two hydroxyl groups. Because the average number of hydroxyl groups per molecule was not known, the cyanomalonate polyesters were reported as having a certain hydroxyl number rather than a certain molecular weight. The values found were above 200 for most polyesters prepared from monomeric glycols but lower for those derived from the higher molecular weight polymeric glycols and the N-substituted 2,2'-iminodiethanols. The lower hydroxyl number of polyesters of higher molecular weight polymeric glycols could be explained by the low proportion of trifunctional cyanomalonate in the polyester molecules. Also, polyesters of the N-substituted 2,2'-iminodiethanols could have low hydroxyl numbers because of salt formation between the ester and amine, which would prevent alkylations from taking place.

Cyanosuccinates

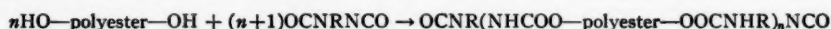
Diethyl cyanosuccinate, which was prepared by condensing the sodium derivative of ethyl cyanoacetate with ethyl chloroacetate (10), proved to be of the same order of reactivity as cyanomalonate, with respect to glycols.

α -Cyanoglutarates

Diethyl α -cyanoglutarate was synthesized by the Michael reaction between ethyl cyanoacetate and ethyl acrylate in the presence of a sodium ethoxide catalyst (11). The ester appeared to be slightly less reactive towards the glycols than was diethyl cyanosuccinate.

Polyurethanes

Polyurethanes were prepared by mixing the hydroxyl-terminated polyesters previously described with various quantities of 2,4-tolylene diisocyanate (TDI) and by allowing the mixture to cure at 100°C for 5 days in the presence of ferric acetylacetonate as a catalyst.



The varied consistencies of the products were classified into different categories, although completely distinct boundary lines did not exist between all of them.

It was found that, in general, more than the equivalent amount of TDI was required to cure a polyester to a solid polyurethane. It was also noted that the polyurethanes tended towards brittle solids as the amounts of TDI increased. The change from stringy to

leathery to resinous was often observed. Also for products which were elastomeric, the elongation at break normally decreased with increasing amount of TDI and in many cases the brittle point increased, although in some cases the reverse was true.

In general, non-elastomeric products were obtained from polyesters of monomeric glycols, while elastomeric polyurethanes with the lowest brittle points were formed from polyoxyethylene glycol 400 and 600 and polyoxypropylene glycol 750, 1025, and 2025 polyesters. Also, in general, the succinate polyurethanes, which did not contain nitrile groups, had the greatest tendency to be elastomeric and had the lowest brittle points (Tables VI and VII). For the nitrile containing polyurethanes, the cyanomalonates had the lowest tendency to be elastomeric and had the highest brittle points (Table VIII). The cyanosuccinates (Table IX) and α -cyanoglutarates (Table X) had about the same properties.

EXPERIMENTAL

Polyesters

Polyesters were prepared by condensing ethylene, diethylene, and triethylene glycols, four polyoxyethylene glycols ranging in molecular weight from 200 to 600, 1,2-propanediol, dipropylene glycol, five polyoxypropylene glycols ranging in molecular weight from 150 to 2025, 1,3-propanediol, 1,3-butanediol, 1,4-butanediol, 2,3-butanediol, 1,5-pentanediol, 2,2'-(methylimino)diethanol, 2,2'-(ethylimino)diethanol, 2,2'-(butylimino)diethanol, and 2,2'-thiodiethanol with diethyl succinate in the absence and presence of a sodium catalyst and with diethyl cyanomalonate (9), cyanosuccinate (10), and α -cyanoglutarate (11).

Equimolar quantities of a glycol and diethyl ester having a combined weight of about 150 grams were placed in a 300-ml three-necked round-bottomed flask. The flask was fitted with thermometer and gas delivery tube in the side necks and Claisen head in the center neck. A vertical condenser protected by a calcium chloride tube was fitted into the side neck of the Claisen head which had a distillate take-off tap mounted at the elbow. The contents of the flask were heated to a temperature in the region of 200° C under a steady stream of nitrogen, ethanol beginning to distill off at reaction temperatures ranging from 95 to 215° C. After a heating period of from 4 to 222 hours, by which time ethanol had ceased to distill, an excess of glycol was added to the reaction mixture in most cases and heating continued for another 4 to 70 hours, at which time ethanol no longer distilled. The contents of the flask, after being allowed to cool, were slowly heated to a temperature in the region of 200° C under a vacuum less than 1 millimeter of mercury for 4 to 12 hours, until no more distillate collected.

The kinematic viscosity of polyesters was measured at 20.0° C using Ostwald-Fenske viscometers. Several determinations were carried out on each sample and the average value computed. Viscosities above 30,000 centistokes were not measured but recorded only as being greater than this value.

The average molecular weight or, in the case of the cyanomalonates, the hydroxyl number of polyesters was determined by a hydroxyl end-group analysis based on acetylation with acetic anhydride in the presence of pyridine. Duplicate determinations were carried out on each polyester and an average taken of the two values obtained.

The individual syntheses of the various polyesters are given in detail as follows: succinates prepared without catalyst, Table I; succinates prepared using sodium catalyst, Table II; cyanomalonates, Table III; cyanosuccinates, Table IV; and α -cyanoglutarates, Table V.

TAB
Succinate polyesters

Starting material					Ethanol collected					Reaction time, hours
Glycol			Diethyl succinate		Reaction temp., °C	Yield				
Name	g	moles	g	moles		Initial temp., °C	Volume, ml	g	%	
Ethylene glycol	46.6	0.75	130.7	0.75	180	180	47	37	53	53
Diethylene glycol	63.7	0.60	104.5	0.60	210	180	54	42	77	16
Triethylene glycol	75.1	0.50	87.1	0.50	210	190	28	22	48	18
PEG* 200	100.0	0.50	87.1	0.50	215	195	13	10	22	90
300	100.0	0.33	58.1	0.33	215	200	17	13	43	40
400	100.0	0.25	43.6	0.25	215	210	10	8	34	40
600	120.0	0.20	34.8	0.20	215	215	5	4	21	127
1,2-Propanediol	49.5	0.65	113.2	0.65	190	190	17	13	22	84
Dipropylene glycol	67.1	0.50	87.1	0.50	210	195	15	12	26	128
PPG* 150	75.0	0.50	87.1	0.50	215	195	12	9	20	123
425	106.3	0.25	43.6	0.25	215	215	5	4	17	197
750	125.0	0.167	29.0	0.167	215	215	4	3	20	197
1,025	128.1	0.125	21.8	0.125	215	215	4	3	27	201
2,025	126.5	0.0625	10.9	0.0625	215	215	2	2	27	222
1,3-Propanediol	57.1	0.75	130.7	0.75	210	180	35	27	46	83
1,3-Butanediol	45.1	0.50	87.1	0.50	200	175	29	23	49	20
1,4-Butanediol	45.1	0.50	87.1	0.50	210	175	42	33	72	8
2,3-Butanediol	45.1	0.50	87.1	0.50	180	180	14	11	24	58
1,5-Pentanediol	52.1	0.50	87.1	0.50	210	190	27	21	46	54
2,2'-(Methylimino)-diethanol	59.6	0.50	87.1	0.50	180	155	36	28	61	21
2,2'-(Ethylimino)-diethanol	66.6	0.50	87.1	0.50	180	165	29	23	49	14
2,2'-(Butylimino)-diethanol	80.6	0.50	87.1	0.50	180	165	25	20	43	27
2,2'-Thiodiethanol	61.1	0.50	87.1	0.50	190	185	22	17	37	36

*Polyoxyethylene glycol (PEG), $\text{HO}(\text{CH}_2)_2\text{O}(\text{CH}_2)_n\text{OH}$, and polyoxypropylene glycol (PPG), $\text{CH}_3\text{CHOHCH}_2\text{OCH}_2\text{CH}_2$ molecular weights were within a 5% tolerance of the values given.

TAB
Succinate polyesters prepared

Starting material						Ethanol collected						Reaction time, hours
Glycol			Diethyl succinate		Sodium catalyst		Reaction temp., °C	Yield		Reaction time, hours		
Name	g	moles	g	moles	g	moles		Initial temp., °C	Volume, ml		g	
Ethylene glycol	46.6	0.75	130.7	0.75	0.50	0.022	180	105	71	56	81	4
Diethylene glycol	63.7	0.60	104.5	0.60	0.50	0.022	210	105	59	46	84	4
Triethylene glycol	75.1	0.50	87.1	0.50	0.50	0.022	210	105	47	37	80	4
PEG 200	100.0	0.50	87.1	0.50	0.50	0.022	210	105	50	39	85	4
300	100.0	0.33	58.1	0.33	0.50	0.022	210	115	32	25	82	5
400	100.0	0.25	43.6	0.25	0.50	0.022	210	120	25	20	85	7
600	100.0	0.167	29.0	0.167	0.50	0.022	210	125	14	11	72	6
1,2-Propanediol	57.1	0.75	130.7	0.75	0.50	0.022	190	110	60	47	68	10
Dipropylene glycol	67.1	0.50	87.1	0.50	0.50	0.022	210	110	43	34	73	4
PPG 150	75.0	0.50	87.1	0.50	0.50	0.022	210	110	44	35	75	4
425	106.3	0.25	43.6	0.25	0.50	0.022	210	130	21	16	72	5
750	125.0	0.167	29.0	0.167	0.30	0.013	210	145	8	6	41	5
1,025	128.1	0.125	21.8	0.125	0.20	0.009	210	155	7	5	48	7
2,025	126.5	0.0625	10.9	0.0625	0.10	0.004	210	145	2	2	27	8
1,3-Propanediol	57.1	0.75	130.7	0.75	0.50	0.022	210	100	73	57	83	4
1,3-Butanediol	45.1	0.50	87.1	0.50	0.50	0.022	200	105	48	38	82	4
1,4-Butanediol	45.1	0.50	87.1	0.50	0.50	0.022	210	100	49	38	83	3
2,3-Butanediol	45.1	0.50	87.1	0.50	0.50	0.022	180	110	32	25	54	10
1,5-Pentanediol	52.1	0.50	87.1	0.50	0.50	0.022	210	100	51	40	87	4
2,2'-(Methylimino)-diethanol	59.6	0.50	87.1	0.50	0.50	0.022	190	105	47	37	80	11
2,2'-(Ethylimino)-diethanol	66.6	0.50	87.1	0.50	0.50	0.022	200	105	40	31	68	11
2,2'-(Butylimino)-diethanol	80.6	0.50	87.1	0.50	0.50	0.022	210	110	42	33	72	4
2,2'-Thiodiethanol	61.1	0.50	87.1	0.50	0.50	0.022	210	105	42	33	72	4

*1,4-Butanediol.

†The product was too dark for an accurate measurement.

LE I

prepared without catalyst

Excess glycol added			Further heating, hours	Total ethanol collected			Reaction mixture heated <i>in vacuo</i>			Weight distillate, g	Polyester		
				Volume, ml	Yield		Final temp., °C	Pressure, mm	Time, hours		Yield, g	Viscosity, cs 20° C	Molecular weight
g	moles	%			g	%							
46.6	0.75	100	30	55	43	62	190	0.1	7	54.0	97.4	Waxy	1,910
63.7	0.60	100	7	54	42	77	210	0.1	7	59.7	112.0	>30,000	2,730
75.1	0.50	100	37	34	27	58	210	0.1	7	67.2	120.5	13,100	1,670
10.0	0.050	10	10	15	12	26	210	0.2	6	15.1	142.9	630	1,120
10.0	0.033	10	10	18	14	46	210	0.5	6	3.0	127.1	990	1,560
10.0	0.025	10	10	11	9	37	210	0.5	6	1.6	130.0	900	1,580
Nil	Nil	Nil	Nil	5	4	21	215	0.2	6	0.1	134.5	Jelly	3,540
49.5	0.65	100	28	19	15	25	190	0.1	7	120.7	53.1	1,230	500
67.1	0.50	100	48	16	13	27	210	0.2	7	56.1	109.8	1,460	840
75.0	0.50	100	70	15	12	26	215	0.2	6	66.5	127.3	600	970
Nil	Nil	Nil	Nil	5	4	17	215	0.2	6	12.6	117.4	240	1,440
Nil	Nil	Nil	Nil	4	3	20	215	0.5	5	11.7	128.3	200	1,250
Nil	Nil	Nil	Nil	4	3	27	215	0.2	6	16.8	110.5	180	1,430
Nil	Nil	Nil	Nil	2	2	27	215	0.2	5	8.9	116.2	350	2,140
57.1	0.75	100	54	46	36	52	210	0.2	7	53.2	120.9	1,380	840
45.1	0.50	100	49	48	38	82	210	0.1	6	5.2	108.6	3,750	1,740
45.1	0.50	100	12	69	54	118	210	0.2	7	7.2	82.6	Waxy	1,900
45.1	0.50	100	46	20	16	34	180	0.5	6	81.6	51.8	560	890
52.1	0.50	100	48	36	28	61	210	0.2	6	21.5	114.8	1,010	840
59.6	0.50	100	7	48	38	82	180	0.1	6	28.6	110.4	>30,000	1,260
66.6	0.50	100	20	42	33	72	180	0.2	6	34.7	126.0	5,910	1,300
80.6	0.50	100	21	34	27	58	180	0.2	6	50.7	141.4	1,620	1,130
61.1	0.50	100	38	40	31	68	190	0.1	6	5.2	160.1	3,890	1,290

(CH₂)_nOCH₂CHOHCH₂. These products were obtained from the Carbide Chemicals Company, Montreal, Que. Their average

LE II

using sodium catalyst

Excess glycol added			Further heating, hours	Total ethanol collected		Reaction mixture heated <i>in vacuo</i>			Weight distillate, g	Polyester			
				Volume, ml	Yield g %	Final temp., °C	Pressure, mm	Time, hours		Yield, g	Viscosity, cs 20° C	Molecular weight	
g	moles	%											
46.6	0.75	100	6	83	65	94	190	0.1	4	41.3	107.1	Waxy	3,620
63.7	0.60	100	8	64	50	91	210	0.2	5	62.6	109.7	>30,000	2,380
75.1	0.50	100	5	54	42	92	210	0.5	4	77.7	107.6	>30,000	2,230
45.1*	0.50	100	5	55	43	94	210	0.6	6	49.0	127.5	~10,000†	1,770
30.0*	0.33	100	7	34	27	87	210	0.5	6	18.8	132.1	~3,000†	1,100
22.5*	0.25	100	4	26	20	89	210	0.5	4	13.7	123.9	~3,000†	1,160
15.0*	0.167	100	7	14	11	72	210	0.5	4	5.8	117.3	~3,000†	1,150
57.1	0.75	100	7	72	57	82	210	0.5	4	56.1	116.9	>30,000	1,630
67.1	0.50	100	12	49	38	83	210	0.5	5	65.4	106.7	>30,000	2,010
75.0	0.50	100	13	51	40	87	210	0.2	6	76.3	113.3	>30,000	2,730
22.5*	0.25	100	12	22	17	75	210	0.2	5	11.0	133.7	~600†	780
15.0*	0.167	100	15	9	7	46	210	0.2	5	9.9	145.1	390	1,120
11.3*	0.125	100	13	7	5	48	210	0.5	6	6.4	141.6	580	1,480
5.6*	0.0625	100	12	2	2	27	210	0.2	5	0.8	133.4	1,370	2,480
57.1	0.75	100	6	86	68	98	210	0.5	4	47.7	122.2	>30,000	1,700
45.1	0.50	100	8	54	42	92	210	0.2	4	40.6	86.4	>30,000	1,220
45.1	0.50	100	6	58	46	99	210	0.5	6	23.2	86.8	Waxy	1,520
45.1	0.50	100	7	37	29	63	180	0.5	6	75.7	64.0	>30,000	670
52.1	0.50	100	6	54	42	92	210	0.5	6	44.8	93.1	>30,000	1,240
59.6	0.50	100	7	60	47	102	180	0.5	5	22.3	108.5	>30,000	2,280
66.6	0.50	100	9	47	37	80	200	0.2	6	38.2	122.3	11,500	1,950
80.6	0.50	100	9	56	44	95	210	0.2	12	49.7	138.5	7,780	2,650
61.1	0.50	100	13	56	44	95	210	0.7	6	11.0	131.8	~10,000†	990

TAB L
Cyanomalonate po

Starting material					Ethanol collected					Reaction time, hours
Glycol			Diethyl cyanomalonate		Reaction temp., °C	Initial temp., °C	Volume, ml	Yield		
Name	g	moles	g	moles				g	%	
Ethylene glycol	37.2	0.60	111.1	0.60	180	100	45	35	64	8
Diethylene glycol	53.1	0.50	92.6	0.50	190	105	43	34	73	8
Triethylene glycol	67.6	0.45	83.3	0.45	200	105	44	35	83	8
PEG 200	80.0	0.40	74.1	0.40	200	105	36	28	77	8
300	90.0	0.30	55.6	0.30	190	105	25	20	71	8
400	80.0	0.20	37.0	0.20	190	105	18	14	77	8
600	90.0	0.15	27.8	0.15	190	105	11	9	62	8
1,2-Propanediol	45.7	0.60	111.1	0.60	180	110	55	43	78	13
Dipropylene glycol	64.4	0.48	88.9	0.48	190	115	42	33	74	8
PPG 150	67.5	0.45	83.3	0.45	190	115	30	24	57	13
425	85.0	0.20	37.0	0.20	190	110	11	9	47	13
750	90.0	0.12	22.2	0.12	190	140	7	5	50	14
1,025	102.5	0.10	18.5	0.10	190	145	6	5	51	14
2,025	101.3	0.050	9.3	0.050	190	145	1	1	17	14
1,3-Propanediol	45.7	0.60	111.1	0.60	190	105	42	33	60	7
1,3-Butanediol	49.6	0.55	101.8	0.55	190	105	46	36	71	7
1,4-Butanediol	49.6	0.55	101.8	0.55	190	95	65	51	101	6
2,3-Butanediol	49.6	0.55	101.8	0.55	180	110	47	37	73	15
1,5-Pentanediol	52.1	0.50	92.6	0.50	190	100	55	43	94	8
2,2'-(Methylimino)-diethanol	59.6	0.50	92.6	0.50	180	105	50	39	85	8
2,2'-(Ethylimino)-diethanol	63.9	0.48	88.9	0.48	180	100	46	36	82	7
2,2'-(Butylimino)-diethanol	64.5	0.40	74.1	0.40	180	110	40	31	85	8
2,2'-Thiodiethanol	61.1	0.50	92.6	0.50	180	95	43	34	73	8

*1,4-Butanediol.

TAB LE
Cyanosuccinate pol

Starting material					Ethanol collected					Reaction time, hours
Glycol		Diethyl cyanosuccinate		Reaction temp., °C	Initial temp., °C	Volume, ml	Yield			
Name	g	moles	g				moles	g	%	
Ethylene glycol	31.0	0.50	99.6	0.50	180	170	30	24	51	8
Diethylene glycol	53.1	0.50	99.6	0.50	210	170	36	28	61	13
Triethylene glycol	75.1	0.50	99.6	0.50	210	190	30	24	51	8
PEG 200	75.0	0.375	74.7	0.375	210	180	28	22	64	14
300	90.0	0.30	59.8	0.30	210	180	22	17	62	14
400	80.0	0.20	39.8	0.20	210	180	15	12	64	14
600	90.0	0.15	29.9	0.15	210	210	8	6	45	21
1,2-Propanediol	38.1	0.50	99.6	0.50	185	180	28	22	48	14
Dipropylene glycol	67.1	0.50	99.6	0.50	210	185	30	24	51	8
PPG 150	75.0	0.50	99.6	0.50	210	185	30	24	51	19
425 I	85.0	0.20	39.8	0.20	210	210	6	5	26	28
425 II	106.3	0.25	49.8	0.25	210	210	7	5	24	29
750 I	90.0	0.12	23.9	0.12	210	210	4	3	28	28
750 II	112.5	0.15	29.9	0.15	210	210	6	5	34	18
1,025 I	102.5	0.10	19.9	0.10	210	210	2	2	17	28
1,025 II	102.5	0.10	19.9	0.10	210	210	2	2	17	26
2,025 I	101.3	0.050	10.0	0.050	210	210	1	1	17	28
2,025 II	121.5	0.060	12.0	0.060	210	210	1	1	14	25
1,3-Propanediol	38.1	0.50	99.6	0.50	200	170	36	28	61	13
1,3-Butanediol	45.1	0.50	99.6	0.50	200	175	31	24	53	21
1,4-Butanediol	45.1	0.50	99.6	0.50	210	165	46	36	78	8
2,3-Butanediol	45.1	0.50	99.6	0.50	175	175	23	18	39	31
1,5-Pentanediol	52.1	0.50	99.6	0.50	210	180	33	26	56	8
2,2'-(Methylimino)-diethanol	59.6	0.50	99.6	0.50	180	110	50	39	85	8
2,2'-(Ethylimino)-diethanol	59.9	0.45	89.6	0.45	180	110	40	31	76	12
2,2'-(Butylimino)-diethanol	60.4	0.375	74.7	0.375	210	110	32	25	73	8
2,2'-Thiodiethanol	55.0	0.45	89.6	0.45	190	155	35	27	66	13

*1,4-Butanediol.

AB
LE III
ate polyesters

Excess glycol added			Further heating, hours	Total ethanol collected		Reaction mixture heated in vacuo				Polyester				
g	moles	%		Volume, ml	Yield		Final temp., °C	Pressure, mm	Time, hours	Weight distillate, g	Yield, g	Viscosity, cs 20° C	Hydroxyl number	Acid number
37.2	0.60	100	6	57	45	81	180	0.1	5	35.3	43.9	>30,000	230	Nil
53.1	0.50	100	6	46	36	78	180	0.4	7	49.7	85.2	>30,000	470	39.6
67.6	0.45	100	7	47	37	89	180	0.4	7	58.1	105.9	>30,000	310	19.0
36.0*	0.40	100	7	63	49	134	180	0.4	7	22.3	79.7	890	240	3.7
27.0*	0.30	100	7	35	27	99	180	0.5	6	14.0	104.3	840	250	2.1
18.0*	0.20	100	7	21	16	89	180	0.4	6	7.8	90.1	830	200	3.1
13.5*	0.15	100	7	12	9	68	180	0.4	6	6.5	97.7	1,050	180	2.0
45.7	0.60	100	7	60	47	85	180	0.5	4	90.3	30.4	>30,000	240	6.6
64.4	0.48	100	7	46	36	82	180	0.3	6	70.2	81.2	>30,000	290	21.2
67.5	0.45	100	7	32	25	61	180	0.2	6	68.1	101.0	>30,000	240	23.3
49.6*	0.20	100	7	17	13	72	180	0.2	6	13.2	90.7	640	220	2.1
10.8*	0.12	100	7	8	6	57	180	0.2	6	4.5	96.7	430	210	25.8
9.0*	0.10	100	7	7	5	60	180	0.1	6	4.2	105.2	500	190	27.2
4.5*	0.05	100	7	1	1	17	180	0.2	6	3.3	102.4	720	91.1	5.5
45.7	0.60	100	7	60	37	67	180	0.5	7	55.6	77.5	>30,000	330	1.3
49.6	0.55	100	7	54	42	84	180	0.4	6	73.5	60.7	>30,000	250	2.0
49.6	0.55	100	6	99	78	153	180	0.5	4	11.7	34.3	>30,000	370	25.9
49.6	0.55	100	11	57	45	88	180	0.3	6	103.6	20.4	>30,000	330	8.3
52.1	0.50	100	8	74	58	126	180	0.4	6	35.8	69.2	5,200	290	9.6
59.6	0.50	100	6	51	40	87	180	0.5	6	65.3	39.0	>30,000	200	Nil
63.9	0.48	100	7	46	36	82	180	0.2	6	75.9	50.1	>30,000	84.2	Nil
64.5	0.40	100	7	41	32	87	180	0.2	5	71.8	57.2	4,650	110	Nil
61.1	0.50	100	7	47	37	80	180	0.4	6	40.9	83.1	2,130	230	Nil

AB
LE IV
ate polyesters

Excess glycol added			Further heating, hours	Total ethanol collected		Reaction mixture heated in vacuo				Polyester			
g	moles	%		Volume, ml	Yield		Final temp., °C	Pressure, mm	Time, hours	Weight distillate, g	Yield, g	Viscosity, cs 20° C	Molecular weight
31.0	0.50	100	6	46	36	78	180	0.1	4	28.4	46.5	>30,000	850
53.1	0.50	100	8	45	35	77	210	0.3	6	59.9	92.6	>30,000	1,360
75.1	0.50	100	14	43	34	73	210	0.5	5	63.1	125.8	>30,000	1,220
33.8*	0.375	100	7	46	36	104	210	0.3	8	39.6	76.3	440	790
27.0*	0.30	100	7	33	26	94	210	0.2	6	15.5	106.1	300	740
18.0*	0.20	100	7	19	15	81	210	0.2	6	5.2	96.5	350	870
13.5*	0.15	100	14	10	8	57	210	0.1	6	9.4	98.3	290	920
38.1	0.50	100	6	35	27	60	185	0.1	4	71.6	35.2	>30,000	1,860
67.1	0.50	100	14	40	31	68	210	0.6	7	84.0	90.1	>30,000	1,140
75.0	0.50	100	14	40	31	68	210	0.5	7	88.2	106.0	>30,000	1,050
18.0*	0.20	100	14	12	9	51	210	0.1	6	35.5	75.1	140	620
Nil	Nil	Nil	Nil	7	5	24	210	0.1	5	8.6	129.7	440	1,340
10.8*	0.12	100	14	5	4	36	210	1.1	6	12.9	91.4	180	840
Nil	Nil	Nil	Nil	6	5	34	210	0.1	7	1.9	129.0	610	1,660
9.0*	0.10	100	14	4	3	34	210	0.1	6	13.0	104.5	230	1,100
Nil	Nil	Nil	Nil	2	2	17	210	0.1	5	1.8	113.4	380	1,770
4.5*	0.05	100	14	1	1	17	210	0.1	6	5.6	102.4	450	1,900
Nil	Nil	Nil	Nil	1	1	14	210	0.2	5	3.4	125.7	580	2,950
38.1	0.50	100	7	47	37	80	200	0.5	6	36.1	73.5	>30,000	1,870
45.1	0.50	100	7	39	31	66	200	0.5	6	64.2	61.7	>30,000	1,080
45.1	0.50	100	13	67	53	114	210	0.1	4	32.5	37.4	Waxy	2,290
45.1	0.50	100	9	24	19	41	175	0.1	5	74.5	57.8	>30,000	630
52.1	0.50	100	10	59	46	100	210	0.1	5	51.3	44.4	840	1,570
59.6	0.45	100	8	56	44	95	180	0.1	7	41.0	92.1	>30,000	1,090
59.9	0.45	100	7	43	34	81	180	0.1	7	42.9	97.0	>30,000	1,120
60.4	0.375	100	8	40	31	91	210	0.1	5	32.5	102.1	21,900	1,580
55.0	0.45	100	7	36	28	68	190	0.2	7	31.2	103.4	6,100	810

TAB L
 α -Cyanoglutarate po

Starting material					Ethanol collected					Reaction time, hours
Glycol		Diethyl α -cyanoglutarate		Reaction temp., °C	Initial temp., °C	Volume, ml	Yield			
Name	g	moles	g				moles	g	%	
Ethylene glycol	31.0	0.50	106.6	0.50	180	175	30	24	51	21
Diethylene glycol	53.1	0.50	106.6	0.50	210	175	44	35	75	13
Triethylene glycol	60.7	0.40	85.3	0.40	210	190	36	28	77	12
PEG 200	80.0	0.40	85.3	0.40	210	190	18	14	38	30
300	100.0	0.33	71.1	0.33	210	190	23	18	59	32
400	100.0	0.25	53.3	0.25	210	190	18	14	61	33
600	100.0	0.167	35.5	0.167	210	210	9	7	46	36
1,2-Propanediol	38.1	0.50	106.6	0.50	190	185	30	24	51	32
Dipropylene glycol	67.1	0.50	106.6	0.50	210	190	27	21	46	35
PPG 150	60.0	0.40	85.3	0.40	210	190	23	18	49	35
425	106.3	0.25	53.3	0.25	215	215	9	7	31	35
750	125.0	0.167	35.5	0.167	215	215	5	4	26	35
1,025	123.0	0.12	25.6	0.12	215	215	4	3	28	35
2,025	141.8	0.070	14.9	0.07	215	215	2	2	24	35
1,3-Propanediol	38.1	0.50	106.6	0.50	200	170	29	23	49	35
1,3-Butanediol	45.1	0.50	106.6	0.50	200	175	44	35	75	32
1,4-Butanediol	45.1	0.50	106.6	0.50	210	170	52	41	89	17
2,3-Butanediol	45.1	0.50	106.6	0.50	180	180	14	11	24	35
1,5-Pentanediol	52.1	0.50	106.6	0.50	210	180	47	37	80	25
2,2'-(Methylimino)- diethanol	59.6	0.50	106.6	0.50	180	120	47	37	80	8
2,2'-(Ethylimino)- diethanol	66.6	0.50	106.6	0.50	180	120	47	37	80	14
2,2'-(Butylimino)- diethanol	64.5	0.40	85.3	0.40	210	120	35	27	75	23
2,2'-Thiodiethanol	55.0	0.45	96.0	0.45	190	155	28	22	53	21

*1,4-Butanediol.

Polyurethanes

A polyester sample (5 or 10 g) was thoroughly mixed in an aluminum foil moisture dish (60 mm diameter, 18 mm depth) with a quantity of 2,4-tolylene diisocyanate, TDI, which was roughly equivalent. The TDI employed contained 100 mg/kg of ferric acetylacetonate as a catalyst. In four other dishes the same amount of polyester was well mixed with quantities of TDI two, three, four, and five times that used for the first sample. Highly viscous polyesters were heated sufficiently that their viscosities were reduced to a few thousand centistokes and solid polyesters melted in order to permit mixing. The moisture dishes and their contents were placed in the oven and allowed to cure for 5 days at 100° C.

The varied consistencies of polyurethane products were classified into several categories, although completely distinct boundary lines did not exist between all of them. The distinguishing features of each category were (a) viscous, the sample was a viscous liquid; (b) stringy, the sample could be drawn out into threads; (c) cheesy, the sample broke cleanly with little or no resistance when a stretching force was applied; (d) gelatinous, the sample was a sticky jelly; (e) elastomeric, the sample recovered its shape on deformation; (f) leathery, the sample was both tough and flexible; on application of a stretching force, it offered resistance but broke without stretching; and (g) resinous, the sample was a brittle solid.

TABLE V
Succinate polyesters

Reaction no.	Excess glycol added			Further heating, hours	Total ethanol collected		Reaction mixture heated <i>in vacuo</i>			Weight distillate, g	Polyester			
	g	moles	%		Volume, ml	Yield		Final temp., °C	Pressure, mm		Time, hours	Yield, g	Viscosity, cs 20° C	Molecular weight
						g	%							
1	31.0	0.50	100	7	37	29	63	180	0.1	5	27.1	72.2	17,100	2,920
2	53.1	0.50	100	13	50	39	85	210	0.2	5	49.1	102.7	>30,000	1,310
3	60.7	0.40	100	21	39	31	83	210	0.2	7	52.2	109.4	~20,000	1,420
4	36.0*	0.40	100	34	29	23	62	210	0.5	5	62.4	69.1	160	540
5	30.0*	0.33	100	35	32	25	82	210	0.5	5	3.3	128.8	230	860
6	22.5*	0.25	100	32	22	17	75	210	0.5	5	2.8	122.1	300	950
7	15.0*	0.167	100	28	9	7	46	210	0.5	5	4.9	113.4	320	1,040
8	38.1	0.50	100	29	42	33	72	190	0.2	6	37.0	70.0	4,200	1,870
9	67.1	0.50	100	36	31	24	53	210	0.2	10	89.6	76.0	>30,000	530
10	60.0	0.40	100	28	25	20	53	210	0.2	10	60.8	108.6	8,780	460
11	22.5*	0.25	100	28	15	12	51	210	0.2	7	49.9	91.4	130	600
12	15.0*	0.167	100	28	8	6	41	210	0.2	6	19.8	127.1	170	890
13	10.8*	0.12	100	28	5	4	36	215	0.2	6	14.4	123.6	230	1,200
14	6.3*	0.070	100	28	2	2	24	210	0.2	6	6.7	140.6	450	2,070
15	38.1	0.50	100	14	40	31	68	200	0.5	7	36.2	79.7	26,100	1,960
16	45.1	0.50	100	29	44	35	75	200	0.1	6	50.7	73.5	~20,000	1,900
17	45.1	0.50	100	35	71	56	121	210	0.2	7	29.4	52.5	130	2,820
18	45.1	0.50	100	21	17	13	29	180	0.5	7	97.7	60.7	370	610
19	32.1	0.50	100	28	65	51	111	210	0.5	7	51.4	60.0	600	1,210
20	39.6	0.50	100	7	53	42	90	180	0.3	6	~70	88.0	14,900	2,120
21	66.6	0.50	100	14	48	38	82	180	0.2	8	63.3	99.9	3,800	2,130
22	64.5	0.40	100	28	37	29	79	210	0.5	8	28.2	116.7	3,360	2,450
23	55.0	0.45	100	13	28	22	53	190	0.1	8	44.2	98.7	1,460	1,480

The elongation at break of elastomeric polyurethanes was determined by measuring the increase in length which a uniform strip of sample (20 mm in length, 1–2 mm in breadth, and 2–4 mm in width) underwent before breaking when a stretching force was applied. Several determinations were made for each value calculated.

The brittle point of elastomeric polyurethanes was determined by measuring the maximum temperature at which a sample (4–5 mm in length, about 1 mm in breadth, and 1–3 mm in width), cooled in an acetone–dry ice bath, broke when a bending force was applied. Many determinations were made for each sample to establish the correct temperature. In some cases, when none of the samples formed from a particular polyester was elastomeric, the brittle point was measured on one of the samples which were either stringy, cheesy, or leathery.

The proportions of 2,4-tolylene diisocyanate and polyester employed to prepare the different polyurethanes are given together with their consistencies, elongations at break, and brittle points as follows: succinate polyurethanes from polyesters prepared without catalyst, Table VI; succinate polyurethanes from polyesters prepared using sodium catalyst, Table VII; cyanomalonate polyurethanes, Table VIII; cyanosuccinate polyurethanes, Table IX; and α -cyanoglutarate polyurethanes, Table X.

TABLE VI
Succinate polyurethanes from polyesters prepared without catalyst

Starting glycol for polyester	TDI per 10 g polyester, g					Consistency of polyurethane		Elongation at break, %		Brittle point, °C	
	1	2	3	4	5	r	r	—	—	—	—
Ethylene glycol						e	e	500	75	-25	—
Diethylene glycol						s	i	—	—	—	—
Triethylene glycol						v	v	—	—	—	—
PEG						v	v	—	—	—	—
200						v	v	—	—	—	—
300						v	v	—	—	—	—
400						v	v	—	—	—	—
600						v	v	—	—	—	—
1,2-Propanediol	2	4	6	8	10	s	r	—	—	—	—
Dipropylene glycol						s	i	—	—	—	—
PPG						s	s	—	—	—	—
150	1	2	3	4	5	v	v	—	—	—	—
425						v	v	—	—	—	—
750						v	v	—	—	—	—
1,025						v	v	—	—	—	—
2,025						v	v	—	—	—	—
1,3-Propanediol	2	4	6	8	10	s	i	—	—	—	—
1,3-Butanediol	1	2	3	4	5	v	v	—	—	—	—
1,4-Butanediol						v	v	—	—	—	—
2,3-Butanediol	2	4	6	8	10	s	r	—	—	—	—
1,5-Pentanediol	2	4	6	8	10	s	e	—	—	—	—
2,2'-(Methylimino)-diethanol	1	2	3	4	5	s	r	—	—	—	—
2,2'-(Ethylimino)-diethanol						s	s	—	—	—	—
2,2'-(Butylimino)-diethanol						s	s	—	—	—	—
2,2'-Thiodiethanol						s	s	—	—	—	—

Note: v, s, e, i, and r signify viscous, stringy, cheesy, elastomeric, leathery, and resinous, respectively.

TABLE VII
Succinate polyurethanes from polyesters prepared using sodium catalyst

Starting glycol for polyester	TDI per 10 g polyester, g	Consistency of polyurethane	Elongation at break, %	Brittle point, °C
Ethylene glycol	0.5 1 1.5 2 2.5	c l l l l	—	—
Diethylene glycol	1 2 3 4 5	s e l l l r	—	—
Triethylene glycol	" "	v c c l l l	—	—
PEG	200	s e l l l l	—	—
300	" "	v s e l l l	150	-33
400	" "	v s e l l l	150	-33
600	" "	v e e l l l	250	-37
1,2-Propanediol	" "	v e e l l l	800	-43
Dipropylene glycol	" "	s e e l l l	100	4
PPG	150	s e e l l r	100	-14
425	" 4 6 8 10	s e l l r r	150	-19
750	1 2 3 4 5	s e l l r r	100	-13
1,025	" "	v s e e e	300	-34
2,025	" "	v s e e e l	200	-52
1,3-Propanediol	" "	s c e e l l	75	-51
1,3-Butanediol	" "	s e e e l r	50	-58
1,4-Butanediol	" "	s e e e l r	400	-27
2,3-Butanediol	" "	s e e l l r	300	-16
1,5-Pentanediol	2 4 6 8 10	s r r l r r	—	—
2,2'-(Methylimino)- diethanol	1 2 3 4 5	s e e l l l	—	—
2,2'-(Ethylimino)- diethanol	" "	s c r r r	450	-59
2,2'-(Ethylimino)- diethanol	" "	s s l r r	—	—
2,2'-(Butylimino)- diethanol	" "	v s l r r	—	—
2,2'-Thiodiethanol	2 4 6 8 10	s e l r r	150	-19

NOTE: v, s, c, e, l, and r signify viscous, stringy, cheesy, elastomeric, leathery, and resinous, respectively.

TABLE VIII
Cyanomalonate polyurethanes

Starting glycol for polyester	TDI per 10 g polyester, g	Consistency of polyurethane	Elongation at break, %	Brittle point, °C
Ethylene glycol	3 6 9	r r r	—	—
Diethylene glycol	4 8 12 16 20	r r r r r	—	—
Triethylene glycol	3 6 9 12 15	s r r r r	—	—
PEG 200	" "	e r r r r	100	—
300	" "	v s s s s	—	—
400	2 4 6 8 10	v s s s s	100	—
600	" "	v s s s s	—	—
1,2-Propanediol	3 6 "	r r r	—	—
Diisopropylene glycol	3 6 9 12 15	r r r r r	—	—
PPG 150	2 4 6 8 10	s e l r r	300	—
425	" "	s s e e e	—	—
750	" "	s s e e e	200	—
1,025	1 2 3 4 5	s s c e c	200	—
2,025	3 6 9 12 15	v e e e e	800	—
1,3-Propanediol	4 8 20	c r r r r	—	—
1,3-Butanediol	3 6 "	s r r	—	—
1,4-Butanediol	3 6 9 12 15	s s r r r	—	—
2,3-Butanediol	3 6 9 12 15	s s r r r	—	—
1,5-Pentanediol	2 4 6 8 10	r r r r r	—	—
2,2'-(Methylimino)- diethanol	1 2 3 4 5	r r s r r	—	—
2,2'-(Ethylimino)- diethanol	" "	r r r r r	—	—
2,2'-(Butylimino)- diethanol	3 6 9 12 15	s r r r r	—	—
2,2'-Thiodiethanol	" "	r r r r r	—	—

NOTE: v, s, c, e, l, and r signify viscous, stringy, cheesy, elastomeric, leathery, and resinous, respectively.

TABLE IX
Cyanosuccinate polyurethanes

Starting glycol for polyester	TDI per 10 g polyester, g	Consistency of polyurethane	Elongation at break, %	Brittle point, °C
Ethylene glycol	2 3 4	r r r	—	—
Diethylene glycol	1 2 "	s s s	—	—
Triethylene glycol	2 4 6	v s s	—	—
PEG 200	8 10	s s s	—	—
300	"	v s s	100	5
400	"	v s s	100	—14
600	"	v s s	100	—19
1,2-Propanediol	1 3 5	s s r	—	—
Dipropylene glycol	1 2 "	s s r	—	—
PPG 150	2 4 6	s s s	—	—
425 I	8 10	s s s	100	13
425 II	1 2 3	s s s	—	—
750 I	4 5	v v s	—	—
750 II	8 10	v v s	100	—2
1,025 I	1 2 3	s s s	—	—
1,025 II	4 5	v v s	100	—17
2,025 I	"	v s s	100	—25
2,025 II	"	v s s	100	—42
1,3-Propanediol	0.5 1 1.5	v s s	50	—31
1,3-Butanediol	2 2.5	v s s	50	—59
1,4-Butanediol	1 2 3	s s s	75	—57
2,3-Butanediol	4 5	s s s	—	—
1,5-Pentanediol	1 2 3	s s s	—	—
2,2'-(Methylimino)- diethanol	2 4	c c c	—	—
2,2'-(Ethylimino)- diethanol	1 2 3	r r r	—	—
2,2'-(Butylimino)- diethanol	"	s s s	—	—
2,2'-Thiodiethanol	2 4 6	s s s	—	—
	8 10	s s s	—	—

NOTE: v, s, c, g, l, and r signify viscous, stringy, cleasy, gelatinous, elastomeric, leathery, and resinous, respectively.

TABLE X
 α -Cyanoglutarate polyurethanes

Starting glycol for polyester	TDI per 10 g polyester, g			Consistency of polyurethane	Elongation at break, %			Brittle point, °C		
Ethylene glycol	1	2	3	4	5	v	s	s	c	4
Diethylene glycol	"	"	"	"	"	s	e	e	e	-15
Triethylene glycol	3	6	9	12	15	v	s	e	e	-15
PEG 200	2	4	6	8	10	v	s	r	r	-2
300	"	"	"	"	"	v	s	s	r	-9
400	1	2	3	4	5	v	s	e	e	-24
600	1	2	3	4	5	s	e	e	e	-26
1,2-Propanediol	3	6	9	12	15	s	e	e	e	-21
Dipropylene glycol	3	6	9	12	15	s	e	e	e	-21
PPG 150	3	4	5	6	9	e	e	e	e	0
425	1	2	3	4	5	v	s	e	e	-3
750	1	2	3	4	5	v	s	e	e	-58
1,025	1	2	3	4	5	v	s	e	e	-39
2,025	"	"	"	"	"	v	s	e	e	-43
1,3-Propanediol	1	1	5	2	2	s	s	s	r	0
1,3-Butanediol	2	4	6	8	10	s	s	e	e	15
1,4-Butanediol	2	3	4	5	6	v	s	s	s	-47
2,3-Butanediol	2	3	4	5	6	v	s	s	s	-11
1,5-Pentanediol	1	2	3	4	5	r	r	r	r	-
2,2'-(Methylimino)- diethanol	"	"	"	"	"	v	s	s	s	-
2,2'-(Ethylimino)- diethanol	"	"	"	"	"	v	s	s	s	-6
2,2'-(Butylimino)- diethanol	"	"	"	"	"	v	s	s	s	-17
2,2'-Thiodiethanol	"	"	"	"	"	v	s	s	s	-1

NOTE: v, s, e, g, i, and r signify viscous, stringy, cheesy, gelatinous, elastomeric, leathery, and resinous, respectively.

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DETERMINATION OF TRACE AMOUNTS OF SILVER IN GALENA ORES¹

E. J. BOUNSALL AND W. A. E. MCBRYDE²

ABSTRACT

An analytical method is described for the determination of microgram amounts of silver in galena ores, based on the "reversion" of silver dithizonate. Silver is separated from relatively large amounts of lead by extraction as dithizonate into chloroform from an aqueous 1:99 nitric acid solution. Separation from mercury, which is also extracted under these conditions and would, if present, interfere in the analysis, is achieved by reverting the dithizonate solution with a 5% aqueous sodium chloride solution which is also 0.015 molar in hydrochloric acid. Following dilution of this aqueous solution and adjustment of pH, silver is again extracted into chloroform as the dithizonate, and determined absorptiometrically. Analyses of a number of galena ore samples showed a precision of within 3% for a silver content ranging from 0.03 to 0.4%.

Some other methods for isolating silver from these samples, which were tried but found unsatisfactory, are discussed.

INTRODUCTION

For an accurate and precise determination of trace amounts of silver in galena ores, a quantitative chemical method of analysis is necessary. Wasserstein (1), having completed a spectrographic analysis of galena (lead sulphide) ores, reported that the sensitivity of detection for the different elements was not the same, and that the role of silver could not be accurately assessed, as its sensitivity in the spectrographic examination did not allow the estimation of even very approximate amounts of this element. Several colorimetric procedures involving extraction and determination of microgram amounts of silver by a chloroform or carbon tetrachloride solution of dithizone have been outlined by Sandell (2). The technique of reversion introduced by Irving, Risdon, and Andrew (3), and later somewhat simplified by Maynes and McBryde (4), in our opinion is an improvement over other published procedures based on the use of dithizone. It eliminates the necessity of using dithizone solutions of exactly known or constant concentration, provides for maximum sensitivity, and is of real value when amounts of interfering metals are present and a reversion agent can be found which will revert the dithizonate of the metal being determined without affecting the other metallic dithizonates.

Since the extraction of lead by dithizone requires an alkaline medium, and since silver, copper, mercury, palladium, and gold are the only metals extracted by dithizone from mineral acid solution, extraction at low pH would be expected to separate silver from the relatively large amounts of lead present in galena, and from any other but the aforementioned elements. Of the latter, gold and palladium are extremely unlikely to be in galena ores, copper is sure to be present, and mercury may possibly be (5). A reversion agent was needed which would not revert copper and mercury, but which would quantitatively revert silver, subsequent to the separation of these metals from lead.

REAGENTS AND APPARATUS

Laboratory distilled water and nitric acid were distilled in borosilicate glass stills. C.P. sulphuric acid and perchloric acid were used without further purification. The 1:99 nitric acid was prepared by dilution of 1 volume of distilled nitric acid with 99 volumes of redistilled water. The 6 N hydrochloric acid was prepared from C.P. concentrated

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Contribution from the Department of Chemistry, University of Toronto, Toronto 5, Ontario, Canada.

²Present address of authors: Department of Chemistry, University of Waterloo, Waterloo, Ontario.

acid, diluted 1:1 with doubly distilled water, and then twice distilled in a borosilicate glass still, with rejection of the first 20% and last 10% of the distillate.

Chloroform

Both U.S.P. and reclaimed chloroform were purified by the procedure outlined by Biddle (6), except that the calcium oxide was filtered out before distillation in a glass still.

Dithizone and Cotton

Purification of each was carried out by the procedure described by Maynes and McBryde (4). Dithizone solutions were prepared by dissolving approximately 10 mg of the purified reagent in 1 liter of chloroform. With experience, solutions of suitable concentration were prepared, by visually estimating the color of the solution, immediately before use.

Buffer and Reversion Agent Solutions

The analytical grade reagents were dissolved in redistilled water, and the solutions shaken with dithizone in chloroform to free them of heavy metals.

Potassium Chromate Solution

A 4% (w/v) solution was prepared from reagent grade potassium chromate and redistilled water.

Standard Solutions of Metals

The composition of these solutions was based on accurately known weights of (i) dried analytical reagent grade silver nitrate; (ii) Specpure lead; (iii) Specpure copper; (iv) doubly distilled mercury. The metals were dissolved in 1:1 nitric acid, and these solutions boiled to free them of oxides of nitrogen; the silver nitrate was dissolved in, and the solutions of all the nitrates made up to, known volumes with 1:99 nitric acid. From stock solutions so prepared, standard solutions of silver, mercury, and copper, containing about 10 μ g of metal (accurately known) per ml, were prepared by dilution with 1:99 nitric acid. The standard lead solution contained about 100 mg of metal (accurately known) per ml.

From time to time, checks were made on the concentration of the standard silver solution by carrying out the reversion procedure described below on a measured volume of this solution. The reversion values for these samples were compared with the standard reversion working curve which had been determined when the solution was first prepared.

Spectrophotometer and Cells

All measurements of optical density were made with a Beckman Model DU spectrophotometer set at 610 m μ , the absorption maximum of dithizone. The optical cells were cylindrical, 1 cm in path length, with Corex glass windows, and ground-glass stoppers to minimize loss of chloroform by evaporation.

Glassware

Borosilicate glassware was used throughout. It was cleaned after each use in hot nitric and sulphuric acids, rinsed thoroughly with tap water, and then washed well with doubly distilled water. Extractions were carried out in Squibb-type separatory funnels. Aliquots of standard metal solutions were measured from 5-ml class A microburettes.

EXPERIMENTAL

Reversion Procedure

A cotton pledget was inserted in the stem of a clean, dry, 125-ml separatory funnel equipped with a 7-mm delivery tube. A measured volume of the standard silver solution

was transferred to the funnel, and the volume made up to 25 ml with 1:99 nitric acid. Sufficient dithizone solution was added to extract all of the silver present, and the funnel was shaken for 1 minute. When the phases separated, the dithizone-dithizonate extract was transferred to a 25-ml volumetric flask. The aqueous phase was washed twice with 8-ml portions of chloroform, and the washings were added to the volumetric flask to make the volume to 25 ml. A portion of this dithizone-dithizonate solution was added to one colorimeter cell. A second portion of approximately 5 to 7 ml was added to a 30-ml separatory funnel, and an equal volume of the reverting solution added. This funnel was shaken for 1 minute, the phases allowed to separate, and a few drops of the reverted dithizone solution allowed to flow through a fresh cotton pledget placed in the stem of the funnel. Sufficient of the reverted solution was then delivered to fill a second colorimeter cell. The spectrophotometer was set to read zero optical density for the first solution, and the apparent optical density of the reverted solution measured against this. This quantity is known as the *reversion value* of the silver solution.

Reversion Agent for Silver

The use of 6% (w/v) potassium iodide in 0.25 *N* sulphuric acid, first recommended as a reversion agent for silver (3), met with little success owing to decomposition of dithizone by free iodine. The addition of 0.1 *N* thiosulphate, suggested by Morrison and Paige (7), did not overcome this difficulty. A neutral 6% (w/v) potassium iodide solution yielded reversion values exhibiting quite poor precision, due perhaps to a solubility loss of dithizone to the neutral reverting medium. Reversions with a 6% (w/v) solution of potassium bromide in 0.1 *N* hydrochloric acid also yielded results with poor precision.

With 2.0 *N* hydrochloric acid as the reversion agent, a series of experiments on amounts of silver solution equivalent to from 5 to 50 μg of metal gave reversion values proportional to the quantity of silver taken. The average reversion value per microgram of silver was 0.0148 ± 0.0001 within a range of 0.0145 to 0.0150. Each reversion value was corrected for a blank amounting to 0.003 ± 0.001 .

Test for Completeness of Extraction of Silver

Maynes and McBryde (4) suggested a convenient test for the completeness of extraction of a metal with dithizone. Applying their procedure, the molar extinction coefficient of dithizone in a chloroform solution was determined, from a solution whose composition was based on a direct weighing of dithizone, to be 3.77×10^4 liter/mole cm. The same quantity was then calculated from the reversion value obtained for a known amount of silver extracted by a known volume of dithizone solution, assuming the molar ratio of silver to dithizone in the dithizonate to be 1:1; this value was 3.94×10^4 liter/mole cm. The difference between the two values is 4%, and the sign of the difference indicates 104% recovery of silver. This difference is attributed to experimental error in the extinction coefficient obtained by direct measurement; the value obtained is somewhat lower than two other published values (4, 8), although the latter were each obtained with different instruments from that used here.

It was concluded that both the extraction of silver with dithizone and the reversion of silver using 2.0 *N* hydrochloric acid were complete; accordingly a standard reversion working curve of reversion plotted against micrograms of silver was prepared for this particular reversion agent and experimental conditions.

Extraction of Other Metals

Comparison with the standard reversion working curve showed that a slight reversion of mercury was also being obtained under the identical reversion conditions used for

silver. In the case of copper, it was found that not even microgram amounts were extracted by dithizone from 1:99 nitric acid, and that no extraction occurred until the pH of the solution was raised by ammonia to 4.2.

Complete extraction of microgram amounts of silver occurred, and no extraction of even microgram amounts from gram quantities of lead was detected at acid concentrations as low as 1:99 nitric acid and 0.1 *N* perchloric acid. Silver was not completely extracted from solutions of perchloric acid more concentrated than 2 normal.

Separation of Silver from Copper and Mercury

In the event that extraction of silver might be required from an acidic medium from which copper was also extracted, a reversion agent was sought which would completely revert silver but not copper or mercury. Friedeberg (9) found that silver could be separated from copper and mercury by selectively decomposing silver dithizonate with a 10% sodium chloride solution which was also 0.015 *N* in hydrochloric acid. The silver was subsequently extracted from this aqueous phase after it had been diluted 10-fold with water, or had its pH raised to between 3 and 3.5, into a solution of dithizone.

To obtain complete recovery of silver by this procedure we have been obliged to modify the directions slightly. The sodium chloride concentration of this reverting solution could be lowered to 5% while the hydrochloric acid concentration was kept unchanged. Copper and mercury dithizonates were completely unreverted by this solution. It was found that the subsequent re-extraction of silver with dithizone was incomplete unless the aqueous phase was both diluted 10-fold and treated to raise its pH to 4.6. The re-extraction of silver was incomplete when the pH was below 4.6 or when the aqueous solution was less dilute regardless of the pH.

Double Reversion Procedure

The recovery of silver and its separation from copper and mercury were tested by the following procedure.

A measured volume of the standard silver solution was transferred to a clean, dry, 125-ml separatory funnel, in the stem of which was a cotton pledget, and the volume made up to 50 ml with 1:99 nitric acid. Sufficient dithizone was added to extract all of the silver present, and the funnel was shaken for 1 minute. When the phases separated, the silver dithizonate-dithizone extract was transferred to another clean, dry, 125-ml separatory funnel, in which were 3 ml of the reversion agent (5% sodium chloride, 0.015 *N* hydrochloric acid). The aqueous phase in the first funnel was washed twice with 5-ml portions of chloroform, and the washings were combined in the second funnel, which was then shaken for 1 minute. When the phases separated, the chloroform phase containing the dithizone was discarded, and the pH of the aqueous phase (containing the silver) was adjusted with sodium acetate solution (1.6 g/liter) to 4.6, and the total volume was made up to 30 ml with redistilled water. Ten milliliters of the dithizone solution was added, and the funnel was shaken for 1 minute. The rest of the procedure was exactly as outlined in the original reversion procedure described above.

This procedure was carried out on amounts of standard silver solution containing the equivalent of from 5 to 45 μg of silver. The average recovery for nine determinations corresponding to 10 μg of silver was 9.97 μg with an average deviation of 0.29 μg . The range of these values was from 9.6 to 10.7 μg after correction for the blank, which was equivalent to 0.7 μg of silver.

Determination of Silver in the Presence of Mercury, Copper, and Lead

Results, corrected for the blank, for the determination of silver, according to the

double reversion procedure, from mixtures of standard solutions of silver, mercury, copper, and lead, in the proportion that these metals are likely to be present in galena ores, are given in Table I.

TABLE I
Results of analyses on make-up samples

	Grams of lead	Micrograms of mercury taken	Micrograms of copper taken	Micrograms of silver	
				Taken	Found
Sample 1	0.5	30	30	30	30.6
" 2	0.5	30	100	30	29.1
" 3	0.5	100	30	30	29.8
" 4	0.5	30	100	15	15.6
" 5	1.0	20	25	45	43.5
" 6	0.5	30	50	20	20.0

Determination of Silver in Galena Ores

The usual method employed for the dissolving of galena ores is heating with hydrochloric acid. However, since even small amounts of chloride prevent the extraction of silver with dithizone, an acid other than hydrochloric must be used. When nitric acid was employed, it was found that, regardless of the temperature (from room temperature to 200° C) or the acid concentration (from concentrated to 1:9) used, a heavy, insoluble, white precipitate of lead sulphate formed during dissolving of the ore. Concentrated perchloric acid, however, at a temperature of 120° to 135° C, was found to be completely satisfactory, with a dissolving time of approximately two hours. When lower acid concentration or lower temperatures were used, a longer time was needed for dissolving. At temperatures above 135° C, regardless of the perchloric acid concentration, a fine white precipitate formed.

Procedure

A sample of ore weighing 0.02 to 0.06 g, after being crushed to a fine powder, was transferred to a 50-ml beaker and covered with a watch glass. Two milliliters of concentrated perchloric acid was added, and the sample heated at 120° to 135° C until dissolution was complete. After the solution was cooled, the watch glass and the sides of the beaker were washed with water, and the solution was evaporated almost to dryness. Sufficient 1:99 nitric acid was added, and the solution was heated just under boiling until all the salts had dissolved. After cooling, the solution was transferred to a 125-ml separatory funnel, and the volume made up to 50 ml with rinsings of 1:99 nitric acid. The double reversion procedure with dithizone was then carried out, and the amount of silver determined by comparison with the standard reversion working curve.

Since there were no standard galena samples available with which to check the accuracy of the new procedure, and since there was no trustworthy alternative procedure of analysis, known amounts ("spikes") of silver were added to various of the ore samples immediately after dissolving, as a means of checking the subsequent analysis. An amount of silver equal to the amount added as the "spike" was then subtracted from the value determined by the analysis.

As the percentage of lead sulphide actually in the ore samples differed widely among the samples, the concentration of silver was expressed as p.p.m. lead, rather than p.p.m. ore sample. A lead analysis for each silver determination was carried out, essentially

according to the chromate procedure outlined by Vogel (10), on the aqueous phase containing the lead from the double reversion procedure. The accuracy and precision of the chromate method for the determination of lead were established by analyzing three 3-ml samples of standard lead solution. The results obtained were 0.4% low, with no deviation.

Galena ore samples obtained from deposits at Broken Hill, N.S.W., Australia, were kindly made available for analysis by Professor R. M. Farquhar, Geophysics Laboratory, Department of Physics, University of Toronto. The results of the analyses, corrected for the blank and "spike", are shown in Table II. The samples marked with asterisks are

TABLE II
Results of galena ore analyses

Sample numbers	Silver in lead (p.p.m.)	Average
667	1211, 1241,* 1197, 1192	1200
668	427, 452, 422*	434
669	1197, 1246, 1247*	1230
670	572, 571, 578, 541*	566
671	699, 734, 711*	715
672	993,* 999, 971	988
723	728, 716, 698	714
725	437, 436, 443	439
726	852, 842, 858	851
912	1780, 1800, 1810	1800
913	3960, 3950	3960
917	307, 293	300

*A "spike" equivalent to 10 micrograms of silver was added.

those to which a "spike" equivalent to 10 micrograms of silver was added. The results of analyses are not listed for 12 samples on which only one determination was made.

The precision of the analyses is within 0.4 to 2.8% based on the average deviation. The determinations on samples to which "spikes" of silver were added do not differ appreciably within the above-stated limits of precision from those analyzed directly.

INVESTIGATION OF OTHER WAYS OF SEPARATING SILVER FROM COPPER AND MERCURY

Extraction of Silver with Diethylammonium Diethyldithiocarbamate

Maynes (11) found that mercury, copper, and only a slight trace of silver could be extracted by a chloroform solution of diethylammonium diethyldithiocarbamate (dithiocarbamate) from aqueous solutions 5.1 *N* in hydrochloric acid. Subsequent dilution of the aqueous phase to 1.5 *N* in hydrochloric acid permitted extraction of silver. A qualitative test for silver in the remaining aqueous phase by means of dithizone revealed no silver.

It was affirmed that no silver was extracted by dithiocarbamate from solutions 5.4 *N* in hydrochloric acid, but that the extraction was still incomplete (50%) when the hydrochloric acid was as dilute as 0.05 *N*. Thus a subsequent determination of silver, after separation of copper and mercury, could not conveniently be achieved if hydrochloric acid was present. Maynes' qualitative test for silver in 1.5 *N* hydrochloric acid employed dithizone, but, as previously described, even small amounts of hydrochloric acid prevent formation of silver dithizonate.

According to Luke (12) silver could be extracted by dithiocarbamate from 3.6 *N*

sulphuric acid. Wyatt (13) reported extraction of copper and mercury by the same reagent from 1 to 10 *N* sulphuric acid solutions. Our results for the extraction of silver by dithiocarbamate from sulphuric acid solutions of differing normality indicate that at low acid concentrations extraction is incomplete, and at high acid concentrations, at which copper and mercury are extracted, silver is as well. Thus a separation of silver from copper and mercury could not be effected.

Extraction with 1,10-Phenanthroline

This reagent forms intensely colored complex ions with iron (II) and copper (I), and the sterically hindered derivatives, 2,9-dimethylphenanthroline (neocuproine) and 2,9-dimethyl-4,7-diphenylphenanthroline (bathocuproine), in chloroform solution have been found specific for microgram amounts of copper (14, 15, 16). The greater selectivity is due presumably to steric hindrance to sixfold co-ordination. Thus, copper might possibly be separable from silver prior to the determination of the latter by the use of these reagents. However, it was found that varying amounts of silver were also extracted by a chloroform solution of 1,10-phenanthroline over the entire pH range below 7. One would expect the derivatives mentioned above to behave in a similar fashion since silver exhibits fourfold co-ordination as a maximum.

Anion Exchange Studies

Attempts with an anion exchange resin of the strongly basic type (Amberlite IRA-400) to remove chloride ion from a silver solution after its separation from mercury and copper (see page 1491) revealed that silver was also completely absorbed by the resin, indicating that silver was present in solution in some anionic form (probably AgCl_2^-).

ACKNOWLEDGMENTS

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17 α -HALOGENATED PROGESTERONES: ORALLY-ACTIVE PROGESTINS¹

DAVID J. MARSHALL AND ROGER GAUDRY

ABSTRACT

17 α -Chloroprogesterone, 6 α -fluoro-17 α -bromoprogesterone, 1-dehydro-6 α -fluoro-17 α -bromoprogesterone, and 6 α -chloro-17 α -bromoprogesterone have been synthesized. These compounds have been found to be orally-active progestins without androgenic properties.

In recent years, considerable effort has been devoted to the search for orally-active progestational agents to substitute for the natural hormone, progesterone. The newer synthetic progestogens which have acquired prominence because of their oral activity fall into two classes: 19-norsteroids such as 19-norprogesterone (1) and 17 α -ethynyl-19-nortestosterone (2) and its Δ^5 (10)-isomer (3), and derivatives of progesterone containing a 17 α -acetoxy substituent (4-7).

It has been shown recently that 17 α -bromoprogesterone (8) is an orally-active progestogen (9), indicating that substituents other than acetoxy at C-17 can enhance the very weak oral activity of progesterone. It was clearly of interest to prepare other 17 α -halogenated progesterones, and to determine whether modifications in structure which enhance the activity of 17 α -acetoxyprogesterone, such as the introduction of a 6 α -halo substituent and a Δ^1 -double bond (4, 5), would have a similar effect on the comparatively weak oral activity of 17 α -bromoprogesterone.

In this paper, we record the synthesis and preliminary biological evaluation of 17 α -chloroprogesterone and of the 6 α -fluoro-, 1-dehydro-6 α -fluoro-, and 6 α -chloro-derivatives of 17 α -bromoprogesterone.

17 α -Chloroprogesterone

Pregnenolone acetate (I) was brominated at a low temperature, and the 5,6-dibromide II was allowed to react with chlorine in acetic acid. The resulting mixture of 17- and 21-chloro derivatives (III) was treated with sodium iodide in acetone which regenerated the 5,6-double bond and replaced chlorine at C-21 with iodine. Finally, the iodine at C-21 was removed by reduction with aqueous sodium bisulphite solution (10) and 17 α -chloropregnenolone acetate (IV, R = Ac) was isolated after chromatographic purification. The α -configuration of the chlorine was inferred from the general preference for "back-side" attack and from the fact that bromination of 20-ketones has been clearly shown to result in the formation of 17 α -bromo derivatives (11).

Acid-catalyzed hydrolysis of IV (R = Ac) yielded 17 α -chloropregnenolone (IV, R = H), which, without purification, was oxidized with chromic acid in acetone (12). The shift of the double bond into conjugation with the carbonyl group to yield 17 α -chloroprogesterone (V) was completed by treatment of the crude oxidation product with oxalic acid (13).

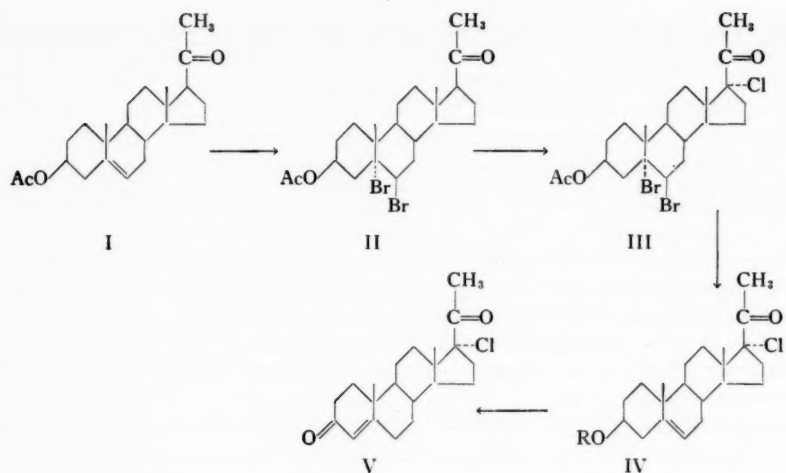
6 α -Halo-17 α -bromoprogesterones²

17 α -Bromopregnenolone acetate (VI) (8, 10) was converted to a 6-fluoro derivative by conventional means (14). Epoxidation of VI with monoperphthalic acid gave a mixture of 5 β ,6 β - and 5 α ,6 α -epoxides, VII and VIII. The epoxides were separated by chromatog-

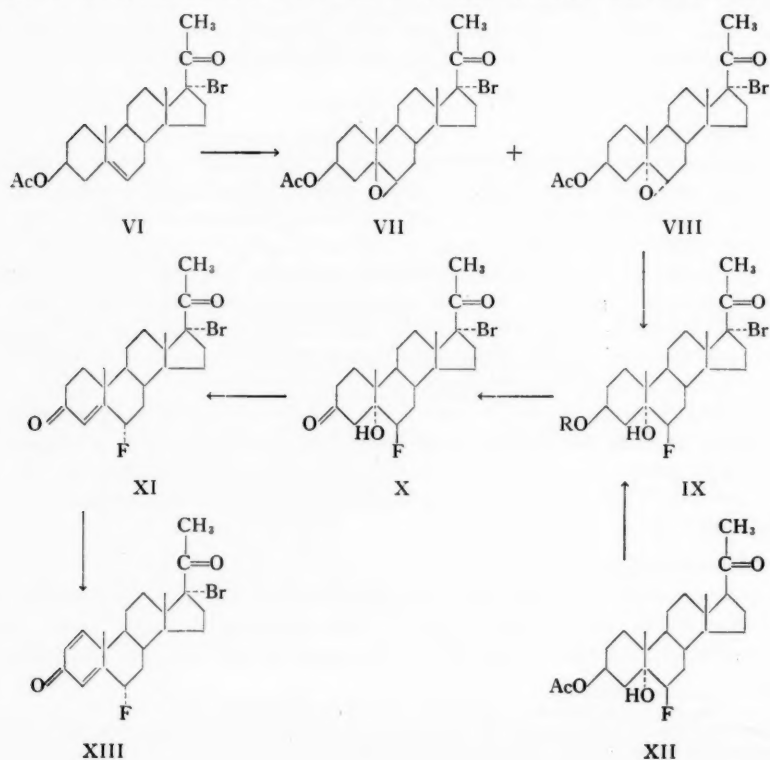
¹Manuscript received May 9, 1960.

Contribution from the Ayerst Research Laboratories, P.O. Box 6115, Montreal, Que.

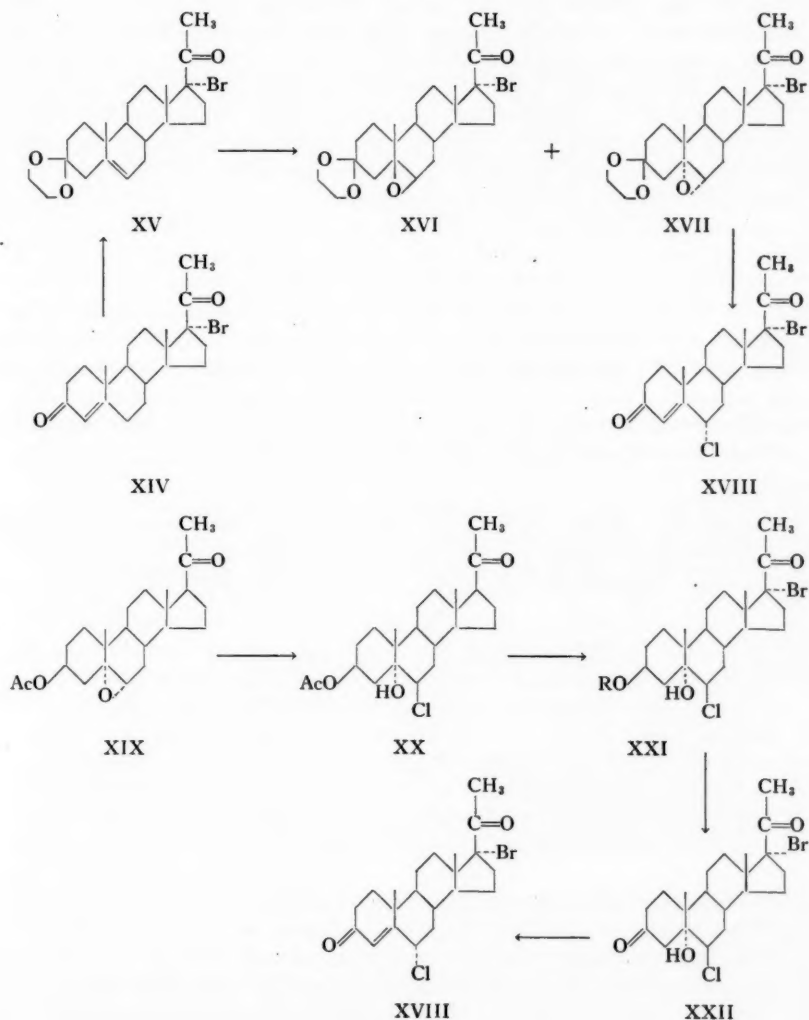
²While this article was in manuscript, the synthesis of 6 α -fluoro-17 α -bromoprogesterone was reported by Ch. R. Engel and R. Deghenghi, *Can. J. Chem.* **38**, 452 (1960).



raphy on Florisil, and the more strongly adsorbed and more levorotatory isomer was assigned the α -structure by analogy with other pairs of epimeric 5,6-epoxides (15). Cleavage of the epoxide ring of VIII with anhydrous hydrogen fluoride (14, 16) gave the



5 α -hydroxy-6 β -fluoro derivative IX (R = Ac) in good yield. The alternative method of forming the fluorohydrin, reaction of the epoxide with boron trifluoride etherate (6, 15, 17-20), gave much less satisfactory results. The fluorohydrin acetate IX (R = Ac) was hydrolyzed with perchloric acid in methanol to the diol IX (R = H). Oxidation of the diol with sodium dichromate in acetic acid and dehydration of the resulting diketone X with anhydrous hydrogen chloride in chloroform gave 6 α -fluoro-17 α -bromoprogesterone (XI), λ_{\max} 237 m μ , ϵ 17,800. The stability of XI to further treatment with acid and the value of the extinction coefficient (6 β -fluoro- Δ^4 -3-ketones have extinction coefficients of 10,000-13,000 (18)) served to establish that the expected inversion of C-6 had occurred, and that the fluorine was in the equatorial (6 α) configuration.



The fluorohydrin IX ($R = \text{Ac}$) was also obtained, in good yield, by bromination of 3 β -acetoxy-5 α -hydroxy-6 β -fluoropregnan-20-one (XII) (16, 17) with N-bromosuccinimide (21).

Dehydrogenation of XI with 2,3-dichloro-5,6-dicyanoquinone (22) yielded the 1-dehydro analogue XIII, which was also obtained, in lower yield, by reaction of XI with selenium dioxide.

For the synthesis of 6 α -chloro-17 α -bromoprogesterone, 17 α -bromoprogesterone (XIV) was converted to the corresponding 3-monoethylene ketal XV by reaction with ethylene glycol and *p*-toluenesulphonic acid in refluxing toluene. Epoxidation of the ketal with monoperphthalic acid gave a mixture of 5 β ,6 β - and 5 α ,6 α -epoxides XVI and XVII, separated by chromatography on Florisil. The configurations of the epoxides were assigned on the basis of their relative behavior during chromatography and a comparison of optical rotations, since it is known (15) that in any pair of epimeric 3-ketal-5,6-epoxides, the α -epoxide is more polar toward adsorbents and is more levorotatory than the β -epimer.

Treatment of the α -epoxide XVII with anhydrous hydrogen chloride in chloroform resulted in cleavage of the epoxide linkage to form the 5 α -hydroxy-6 β -chloro derivative, hydrolysis of the ketal group, dehydration to the α , β -unsaturated ketone, and inversion of configuration at C-6, and 6 α -chloro-17 α -bromoprogesterone (XVIII) was isolated in 80% yield. The structure of XVIII was established by elemental analysis, by infrared and ultraviolet spectral data, and by the stability of the compound to acid.

In a second synthesis of XVIII, 3 β -acetoxy-5 α ,6 α -epoxypregnan-20-one (XIX) (16, 17) was allowed to react with hydrogen chloride in chloroform, and the resulting 5 α -hydroxy-6 β -chloro derivative XX was brominated at C-17 with N-bromosuccinimide to give XXI ($R = \text{Ac}$). Acid-catalyzed hydrolysis to the diol XXI ($R = \text{H}$), oxidation to the diketone XXII, and dehydration-inversion with hydrogen chloride then led to XVIII.

A crystalline product could not be obtained from attempted dehydrogenations of XVIII with selenium dioxide or 2,3-dichloro-5,6-dicyanoquinone.

Biological Activity

The progestational activity of the 17 α -halogenated progesterones relative to progesterone (subcutaneous) and to 17 α -ethynyl-19-nortestosterone (oral), as determined in the Clauberg assay, is summarized in Table I. It will be seen that chlorine has a smaller

TABLE I
Relative progestational activity (Clauberg assay)

	Subcutaneous	Oral
Progesterone	1.0	
17 α -Ethynyl-19-nortestosterone		1.0
17 α -Bromoprogesterone (XIV)	2.0	0.04
17 α -Chloroprogesterone (V)	1.0	<0.04
6 α -Fluoro-17 α -bromoprogesterone (XI)	4.0	0.3
6 α -Chloro-17 α -bromoprogesterone (XVIII)	2.0	0.3

potentiating effect on the progestational activity than does bromine at C-17 α of progesterone. But fluorine and chlorine at C-6 α enhance the activity of 17 α -bromoprogesterone to about the same extent as they enhance the activity of 17 α -acetoxyprogesterone (6, 7). Preliminary assays indicated that the 1-dehydro derivative XIII was more active than XI.

There have been a number of reports recently that the administration of some synthetic progestins to rats (23) and to humans (24) during gestation can induce masculinization of female fetuses. For example, it has been found (23) that when pregnant rats are treated with relatively low doses of 17 α -ethynyl-19-nortestosterone or 6 α -methyl-17 α -acetoxyprogesterone (5), serious masculinization occurs in the female offspring. It was therefore of interest to test some of the compounds made in this investigation for androgenic activity. The 17 α -bromoprogesterones did not show androgenic properties in castrated male rats, nor was there any indication of masculinization in female offspring of pregnant rats which had been treated with high doses of XI or XIV.

The detailed results of the biological assays of these compounds will be published elsewhere (25).

EXPERIMENTAL

Melting points are uncorrected. Rotations were determined in chloroform solution at a concentration of about 1%, and ultraviolet spectra were taken in solution in 95% ethanol. The alumina used for chromatography was Merck chromatographic grade alumina which had been neutralized by being allowed to stand overnight in ethyl acetate and reactivated by heating *in vacuo* at 145° for 18 hours. Microanalyses were carried out in our analytical laboratory by Mr. W. J. Turnbull and associates.

17 α -CHLOROPROGESTERONE

17 α -Chloropregnenolone Acetate (IV, R = Ac)

To a stirred solution of 50.0 g of 3 β -acetoxy-5-pregnen-20-one in 930 ml of chloroform cooled to -60° was added over a period of 2 hours 467 ml of a 0.3 M solution of bromine in carbon tetrachloride. After the solution was warmed to room temperature, the volume was reduced to about 100 ml *in vacuo* and the 5 α ,6 β -dibromide II was precipitated by the addition of 350 ml of methanol. The yield was 60.4 g, m.p. 143-146° decomp.

To a solution of 14.0 g of II in 125 ml of acetic acid containing 0.1 ml of concentrated hydrochloric acid was added 78.4 g of a solution of chlorine in acetic acid (2.46 g chlorine per 100 g of solution) over a period of 1 hour. After 250 ml of water was added, the mixture was refrigerated overnight and the colorless solid was filtered and washed with water. Crystallization from methylene chloride-methanol yielded 10.3 g of a mixture of 17- and 21-chlorodibromides (III), m.p. 129-137° decomp. This product was dissolved in 100 ml of boiling acetone and a solution of 10 g of sodium iodide in 60 ml of acetone was added. After it was heated under reflux for 1 hour, under nitrogen, the mixture was cooled in ice and the iodine was reduced by the slow addition of 362 ml of 0.1 N sodium thiosulphate solution. The precipitated product was dissolved in 70 ml of ether, 10 ml of 10% sodium bisulphite solution was added, and the mixture was shaken intermittently for 30 minutes, after which no further iodine color developed on standing. The ether solution was washed with an additional portion of bisulphite solution and with water and was dried and concentrated to dryness. The resulting solid (6.8 g) could not be readily purified by crystallization.

A 1.87 g portion of this product was chromatographed on 65 g of alumina. Elution with 650 ml of benzene-petroleum ether 1:3 yielded 1.45 g of 3 β -acetoxy-17 α -chloro-5-pregnen-20-one (IV, R = Ac); m.p. 145-148°. Crystallization from methylene chloride-methanol gave an analytical sample, m.p. 147-149°, $[\alpha]_D$ -84.9°. Anal. Calc. for C₂₃H₃₃ClO₂: C, 70.30; H, 8.46; Cl, 9.02. Found: C, 70.41; H, 8.67; Cl, 9.18.

17 α -Chloroprogesterone (V)

A mixture of 4.65 g of the acetate IV ($R = \text{Ac}$), 130 ml of methanol, and 4.65 ml of 70% perchloric acid was heated at the boiling point until the solid had dissolved and was then left at room temperature for 24 hours. Water (140 ml) precipitated 3.80 g of 17 α -chloropregnenolone (IV, $R = \text{H}$), m.p. 120°, resolidifying and remelting at 156–161°, which was not further purified.

To a stirred solution of 3.48 g of 17 α -chloropregnenolone in 140 ml of acetone cooled to 5° under nitrogen was added 2.78 ml of a chromic acid solution (26.72 g of chromium trioxide in 23 ml of sulphuric acid diluted to 100 ml with water). After the solution had been stirred for 5 minutes, 420 ml of water was added and the precipitated solid was filtered and dried (3.25 g). This product was dissolved in 43 ml of ethanol, 1.6 g of oxalic acid was added, and the solution was heated under reflux under nitrogen for 45 minutes. Water was added and the product was extracted with ether. The ether solution was washed with 5% sodium bicarbonate solution and with water, and the brown gum remaining after drying and evaporation of the solvent was adsorbed on 150 g of alumina in benzene – petroleum ether 1:1. Elution with 600 ml of benzene gave 1.14 g of colorless solid which was crystallized from aqueous methanol yielding 1.00 g of 17 α -chloroprogesterone (V), m.p. 166–168°. Recrystallization from aqueous methanol gave an analytical sample, m.p. 168.5–170°, $[\alpha]_D + 51.0^\circ$, λ_{max} 240 m μ (ϵ 17,900). Anal. Calc. for $\text{C}_{21}\text{H}_{29}\text{ClO}_2$: C, 72.31; H, 8.38; Cl, 10.12. Found: C, 72.63; H, 8.39; Cl, 10.31.

6 α -FLUORO-17 α -BROMOPROGESTERONE*Epoxidation of 17 α -Bromopregnenolone Acetate*

To a stirred, ice-cooled solution of 5.00 g of 3 β -acetoxy-17 α -bromo-5-pregnen-20-one in 75 ml of chloroform was added, over a period of 15 minutes, 102 ml of a 0.342 *M* solution of monoperphthalic acid in ether. After storage at 10° for 4 days, the mixture was filtered, and the filtrate was washed with 10% sodium bicarbonate solution and with water and dried over magnesium sulphate. The crude product obtained after evaporation of the solvent was dissolved in benzene and chromatographed on 150 g of Florisil. Two liters of benzene containing 1% ethyl acetate eluted 1.12 g of the 5 β ,6 β -epoxide VII, which was recrystallized from ethyl acetate, m.p. 158–160.5°, $[\alpha]_D - 57.6^\circ$. Anal. Calc. for $\text{C}_{23}\text{H}_{33}\text{BrO}_4$: C, 60.92; H, 7.34; Br, 17.62. Found: C, 61.15; H, 7.22; Br, 17.57.

Elution of the column with 2 liters of benzene containing 5% ethyl acetate gave 2.82 g of the 5 α ,6 α -epoxide VIII, which, after recrystallization from ethyl acetate had a melting point of 192–193°, $[\alpha]_D - 102.4^\circ$. Anal. Calc. for $\text{C}_{23}\text{H}_{33}\text{BrO}_4$: C, 60.92; H, 7.34; Br, 17.62. Found: C, 60.64; H, 7.12; Br, 17.31.

*3 β -Acetoxy-5 α -hydroxy-6 β -fluoro-17 α -bromopregnan-20-one (IX)**A. From the Epoxide VIII*

To 51.1 g of anhydrous hydrogen fluoride in a polyethylene bottle in a Dry Ice-acetone bath at -60° was added slowly, in turn, 102 g of dry tetrahydrofuran, 50 ml of chloroform, and a solution of 51.1 g of the epoxide VIII in 325 ml of chloroform. The solution was kept at -10° for 2 hours and was then poured, with stirring, into a mixture containing 200 g of potassium carbonate, 600 ml of water, ice, and 100 ml of chloroform. The chloroform solution was washed with sodium bicarbonate solution and with water, dried over magnesium sulphate, and evaporated to dryness *in vacuo*. Crystallization from methylene chloride – methanol yielded 34.7 g of the fluorohydrin IX, m.p. 170–171° decomp. The analytical sample, obtained by crystallization from the same solvent

mixture had a melting point of 173° decomp., $[\alpha]_D -78.3^\circ$. Anal. Calc. for $C_{23}H_{34}BrFO_4$: C, 58.34; H, 7.24; Br, 16.88; F, 4.01. Found: C, 58.32; H, 7.26; Br, 16.85; F, 3.89.

B. From 3 β -Acetoxy-5 α -hydroxy-6 β -fluoropregnan-20-one (XII)

A mixture of 20.0 g of the fluorohydrin XII, 15.0 g of N-bromosuccinimide, and 500 ml of carbon tetrachloride was heated under reflux on the steam bath. When the solvent was boiling vigorously, the flask was irradiated with a 250-watt infrared lamp and refluxing was continued for 10 minutes. The flask was then cooled in an ice bath, the mixture was filtered, and the filtrate was washed with dilute sodium bisulphite solution and with water. The dried (Na_2SO_4) solution was evaporated to dryness *in vacuo* and 40 ml of methanol was added to the amorphous residue. The mixture was brought rapidly to the boiling point, cooled in ice, and the crystalline product was filtered and washed with methanol. The yield of 17 α -bromo derivative IX was 15.1 g, m.p. 171.5° decomp., identical (mixed m.p. and infrared spectrum) with the product obtained in A.

In larger runs it was found desirable to have a small amount of pyridine present to inhibit the ionic bromination which sometimes occurred. Thus, a mixture of 100 g of IX, 75 g of N-bromosuccinimide, 2.5 liters of carbon tetrachloride, 24 g of pyridine, and 6 g of benzoyl peroxide heated under reflux for 15 minutes followed by working up as above, yielded 80 g of VI, m.p. 174° decomp.³

3 β ,5 α -Dihydroxy-6 β -fluoro-17 α -bromopregnan-20-one (IX, R = H)

A mixture of 34.7 g of the acetate IX (R = Ac), 500 ml of methanol, and 12 ml of 70% perchloric acid was boiled until the steroid had dissolved (about 10 minutes) and was then left at room temperature for 17 hours. The solid obtained by the addition of 500 ml of water was crystallized from methanol, yielding 25.8 g of the diol IX (R = H), m.p. 174° decomp. Recrystallization from aqueous methanol gave the analytical sample, m.p. 176° decomp., $[\alpha]_D -65.2^\circ$. Anal. Calc. for $C_{21}H_{32}BrFO_3$: C, 58.46; H, 7.48; Br, 18.52; F, 4.40. Found: C, 58.22; H, 7.71; Br, 18.44; F, 4.56.

5 α -Hydroxy-6 β -fluoro-17 α -bromopregnane-3,20-dione (X)

To a solution of 25.8 g of the diol IX (R = H) in 250 ml of acetic acid cooled to 15° was added with stirring a solution of 25.8 g of sodium dichromate dihydrate in 520 ml of acetic acid. After the mixture had been allowed to stand at room temperature for 16 hours, 50 ml of methanol was added, followed by 1300 ml of water. The finely divided solid was filtered and washed well with water. The wet product, which was difficult to dry, was dissolved in methylene chloride (in which it was only moderately soluble), and the solution was dried over sodium sulphate and concentrated. Crystallization from methylene chloride - methanol yielded 16.4 g of the diketone X, m.p. 174° decomp., and 2.8 g, m.p. 173° decomp. The analytical sample, m.p. 173.5-174.5° decomp., $[\alpha]_D -42.1^\circ$, was obtained by crystallization from *i*-propanol. Anal. Calc. for $C_{21}H_{30}BrFO_3$: C, 58.75; H, 7.04; Br, 18.61; F, 4.93. Found: C, 58.71; H, 6.91; Br, 18.90; F, 4.49.

6 α -Fluoro-17 α -bromoprogesterone (XI)

Anhydrous hydrogen chloride was passed for 1 hour through an ice-cooled suspension of 10.8 g of the diketone X in 200 ml of chloroform. The solid went rapidly into solution. After standing an additional hour in the ice bath, the orange solution was washed with water, 10% sodium bicarbonate solution, and again with water. Drying over sodium sulphate and evaporation of the solvent gave a solid which was crystallized from methylene chloride - methanol, yielding 6.5 g of 6 α -fluoro-17 α -bromo-4-pregnene-3,20-dione

³We are indebted to Dr. Gordon Myers for carrying out this experiment.

(XI) as colorless needles, m.p. 173–175.5° decomp. From the mother liquors, an additional 0.5 g of product was obtained, m.p. 171–173° decomp. Recrystallization from methylene chloride – methanol yielded an analytical sample, m.p. 176–177.5° decomp., $[\alpha]_D +17.0^\circ$, λ_{\max} 236 m μ (ϵ 17,800). Anal. Calc. for $C_{21}H_{28}BrFO_2$: C, 61.34; H, 6.86; Br, 19.43; F, 4.62. Found: C, 61.51; H, 7.06; Br, 19.28; F, 4.42.

1-Dehydro-6 α -fluoro-17 α -bromoprogesterone (XIII)

A solution of 1.00 g of XI, 0.64 g of 2,3-dichloro-5,6-dicyanoquinone (22), and 26 mg of *p*-toluenesulphonic acid in 40 ml of benzene was heated under reflux for 18 hours. The cooled mixture was filtered, and the filtrate was diluted with 20 ml of ethyl acetate and washed (initially without shaking to avoid emulsions) with 10% sodium bicarbonate solution and with water. After drying over magnesium sulphate, the solvent was removed *in vacuo*, and the solid residue was chromatographed in benzene on 10 g of Florisil. Elution with 250 ml of benzene containing 5–10% ethyl acetate yielded 656 mg of pale yellow solid. Crystallization from methylene chloride – methanol (charcoal) gave 0.51 g of XIII as colorless plates, m.p. 181–182° decomp. The analytical sample was obtained by recrystallization from acetone–hexane and melted at 181–183° decomp., $[\alpha]_D -20.5^\circ$, λ_{\max} 241 m μ (ϵ 18,200), $\nu_{\max}^{CS_2}$ 1711 cm^{-1} (20-ketone), 1675 cm^{-1} (3-ketone), 1637 cm^{-1} ($\begin{smallmatrix} \diagup & & \diagdown \\ C=C & & \\ \diagdown & & \diagup \end{smallmatrix}$), 904 cm^{-1} . Anal. Calc. for $C_{21}H_{26}BrFO_2$: C, 61.63; H, 6.40; Br, 19.53; F, 4.64. Found: C, 61.52; H, 6.31; Br, 19.38; F, 4.78.

6 α -CHLORO-17 α -BROMOPROGESTERONE

3,3-Ethylenedioxy-17 α -bromo-5-pregnen-20-one (XV)

A mixture of 10.0 g of 17 α -bromoprogesterone, 310 ml of toluene, 80 ml of ethylene glycol, and 0.30 g of *p*-toluenesulphonic acid was heated under reflux under a water separator for 6 hours. After it was cooled in ice, the mixture was washed with 10% sodium bicarbonate solution and with water, and the solvent was removed *in vacuo*. Crystallization from methanol containing a few drops of pyridine yielded 5.0 g of the 3-ketal XV, m.p. 128–130°. The analytical sample was obtained by crystallization from methanol, m.p. 131–132°, $[\alpha]_D -84.0^\circ$. The infrared spectrum (CS_2) showed a single carbonyl band at 1705 cm^{-1} . Anal. Calc. for $C_{23}H_{33}BrO_3$: C, 63.16; H, 7.60; Br, 18.27. Found: C, 63.40; H, 7.60; Br, 18.56.

Epoxidation of XV

To a solution of 2.00 g of the bromoketal XV in 40 ml of chloroform cooled to -60° was added 47 ml of a 0.192 *M* solution of monoperphthalic acid in ether over a period of 20 minutes. After it had been stirred at -60° for 2 hours, the mixture was kept overnight at 0° , washed with 5% sodium carbonate solution and with water, dried over magnesium sulphate, and the solvent was removed. The crude product was chromatographed in benzene on 60 g of Florisil. Elution with benzene containing 2% ether gave the 5 β ,6 β -epoxide XVI, which was crystallized from methanol, yielding 0.70 g, m.p. 119–120°. Recrystallization from methanol gave an analytical sample, m.p. 120–121°, $[\alpha]_D -38.4^\circ$. Anal. Calc. for $C_{23}H_{33}BrO_4$: C, 60.92; H, 7.33; Br, 17.63. Found: C, 60.69; H, 7.23; Br, 17.74.

The 5 α ,6 α -epoxide XVII was obtained by elution of the column with benzene containing 10% ether. Crystallization from methanol gave 0.69 g of XVII, m.p. 180–182°. The analytical sample, obtained by recrystallization from methanol, had m.p. 182–183°.

$[\alpha]_D -88.4^\circ$. Anal. Calc. for $C_{23}H_{33}BrO_4$: C, 60.92; H, 7.33; Br, 17.63. Found: C, 60.72; H, 7.25; Br, 17.62.

3 β -Acetoxy-5 α -hydroxy-6 β -chloropregnan-20-one (XX)

Hydrogen chloride was passed for 1 hour through a solution of 122 g of 3 β -acetoxy-5 α ,6 α -epoxypregnan-20-one (XIX) (18, 19) in 1 liter of chloroform. After an additional hour at room temperature, the solution was washed with water, 10% sodium bicarbonate solution, and water again, and dried over sodium sulphate. Removal of the solvent and crystallization from methylene chloride-methanol yielded two crops of XVI totalling 101 g, m.p. 230–233° decomp. Recrystallization from the same solvent combination raised the m.p. to 232–234° decomp., $[\alpha]_D +8.1^\circ$. Anal. Calc. for $C_{23}H_{35}ClO_4$: C, 67.22; H, 8.58; Cl, 8.63. Found: C, 67.41; H, 8.49; Cl, 8.67.

3 β -Acetoxy-5 α -hydroxy-6 β -chloro-17 α -bromopregnan-20-one (XXI, R = Ac)

A suspension of 101 g of the chlorohydrin XX and 101 g of N-bromosuccinimide in 2.6 liters of carbon tetrachloride was heated to the boiling point and irradiated with two 250-watt heat lamps for 15 minutes. The mixture was then cooled in ice and filtered, and the filtrate was washed with 5% sodium bisulphite solution, 10% sodium bicarbonate solution, and water. Drying over sodium sulphate and evaporation of the solvent *in vacuo* gave a crude product, which, on crystallization from aqueous methanol, yielded 80 g of XXI (R = Ac), m.p. 188–190° decomp. The analytical sample, m.p. 190–191° decomp., $[\alpha]_D -66.1$, was obtained by recrystallization from aqueous methanol. Anal. Calc. for $C_{23}H_{34}BrClO_4$: C, 56.39; H, 7.00. Found: C, 56.10; H, 6.92.

3 β ,5 α -Dihydroxy-6 β -chloro-17 α -bromopregnan-20-one (XXI, R = H)

Eighty grams of the acetate XXI (R = Ac) was dissolved in 2 l. of methanol by warming and 50 ml of 70% perchloric acid was added. The solution was left overnight at room temperature and the product was then precipitated by the addition of 1 liter of water. The yield of diol XXI (R = H) was 54 g, m.p. 175° decomp. After recrystallization from acetone-hexane, the diol melted at 175.5° decomp., $[\alpha]_D -70.7^\circ$, but it did not give a satisfactory analysis. Anal. Calc. for $C_{21}H_{32}BrClO_3$: C, 56.31; H, 7.20. Found: C, 56.94; H, 7.00.

5 α -Hydroxy-6 β -chloro-17 α -bromopregnane-3,20-dione (XXII)

To a solution of 51.5 g of diol XXI (R = H) in 515 ml of acetic acid was added a solution of 25.75 g of sodium dichromate in 515 ml of acetic acid. The mixture was left for 4 hours at room temperature, 2 liters of water was added, and the precipitated solid was filtered and washed with water. The yield of diketone XXII was 42 g, m.p. 188–190° decomp. The analytical sample, m.p. 190° decomp., $[\alpha]_D -62.2^\circ$, was obtained by recrystallization from *i*-propanol. Anal. Calc. for $C_{21}H_{30}BrClO_3$: C, 56.57; H, 6.78. Found: C, 56.58; H, 6.75.

6 α -Chloro-17 α -bromoprogesterone (XVIII)

A. From the Epoxyketal XVII

Hydrogen chloride was passed for 1 hour through a solution of 1.3 g of XVII in 30 ml of chloroform. After it had been allowed to stand an additional hour, the solution was washed with water, with 5% sodium carbonate solution, and with water again and dried over magnesium sulphate. The product obtained on evaporation of the solvent was crystallized from acetone-hexane, yielding 0.98 g of 6 α -chloro-17 α -bromo-4-pregnene-3,20-dione (XVIII), m.p. 156–157°. Recrystallization from the same solvent mixture gave

an analytical sample, m.p. 157–158°, $[\alpha]_D +6.5^\circ$, λ_{\max} 237 m μ (ϵ 16,200). Anal. Calc. for $C_{21}H_{28}BrClO_2$: C, 58.96; H, 6.60. Found: C, 59.02; H, 6.40.

B. From the Hydroxyketone XXII

An ice-cooled suspension of 3.0 g of XXII in 75 ml of chloroform was treated with hydrogen chloride for 1 hour, and, after an additional hour, the product was isolated as in *A*. Crystallization from acetone–hexane yielded 2.3 g of XVIII, m.p. 152–153°, identical by mixed m.p. and infrared spectrum with the product obtained in *A*.

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SOME DEUTERIUM KINETIC ISOTOPE EFFECTS

II. α -DEUTERIUM EFFECTS IN THE WATER SOLVOLYSIS OF SOME ALKYL COMPOUNDS¹

K. T. LEFFKE,² J. A. LLEWELLYN,² AND R. E. ROBERTSON

ABSTRACT

As an extension of previous work on methyl compounds, α -deuterium kinetic effects have been measured for ethyl, *n*-propyl, and isopropyl compounds. The effects can be accounted for in terms of current theory but a modification involving intramolecular van der Waals forces seems to provide a more satisfactory description of some of the processes involved in the production of the rate changes.

INTRODUCTION

When deuterium is substituted for a protium in compounds undergoing nucleophilic substitution reactions, the kinetic isotope effects (measured as the rate ratio k_H/k_D) may be greater or less than unity, i.e. deuteration may produce an increase or a decrease in rate of reaction (1). The reaction which we have studied is a simple hydrolysis in water symbolized by



where X, the leaving group, may be bromine, iodine, benzenesulphonate, substituted benzenesulphonate, or methanesulphonate. Earlier studies on a series of methyl compounds showed that increased reaction velocities were characteristic of the heavy analogues (2) but in this extension of that work we find effects in both directions when more complicated molecules are examined. The reaction rates were determined conductimetrically and the Guggenheim analysis (3) applied to the data to give pseudo-first order rate constants; the experimental techniques have been described in more detail elsewhere (4). Rate data are given in Table I. Several of the light analogues of the compounds examined in this investigation had already been studied and our current measurements are in excellent agreement with this data previously determined in this laboratory.¹

TABLE I

Deuterium isotope effect for more complicated compounds hydrolyzing in water

Compound	Solvolytic rates		<i>T</i> (°C)	k_H/k_D
	Protium compound ($k_1 \text{ sec}^{-1}$)	α -Deuterated compound ($k_1 \text{ sec}^{-1}$)		
Ethyl <i>p</i> -toluenesulphonate	1.998×10^{-4}	1.925×10^{-4}	54.285	1.03 ₃
Ethyl methanesulphonate	1.957×10^{-4}	1.888×10^{-4}	60.003	1.03 ₇
Ethyl bromide	2.722×10^{-4}	2.769×10^{-4}	80.001	0.98 ₈
Ethyl iodide	1.554×10^{-4}	1.625×10^{-4}	80.000	0.96 ₈
Isopropyl <i>p</i> -toluenesulphonate	7.664×10^{-4}	6.757×10^{-4}	30.001	1.13 ₄
Isopropyl methanesulphonate	3.690×10^{-4}	3.229×10^{-4}	29.999	1.14 ₃
Isopropyl bromide	3.493×10^{-4}	3.269×10^{-4}	59.998	1.06 ₉
Isopropyl iodide	3.115×10^{-4}	2.967×10^{-4}	59.996	1.05 ₆
<i>n</i> -Propyl benzenesulphonate	2.042×10^{-4}	1.974×10^{-4}	54.192	1.03 ₄
<i>n</i> -Propyl methanesulphonate	1.370×10^{-4}	1.322×10^{-4}	60.004	1.03 ₄
<i>n</i> -Propyl bromide	1.629×10^{-4}	1.663×10^{-4}	80.009	0.98 ₉
<i>n</i> -Propyl iodide	2.230×10^{-4}	2.217×10^{-4}	90.003	1.00 ₄

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²National Research Council Postdoctorate Fellow.

DISCUSSION

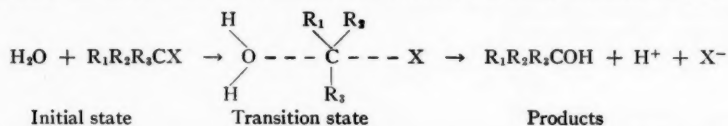
The general theory advanced for the α -deuterium effects observed with methyl compounds involved two opposing changes, both of which affected the frequencies of the fundamental modes of vibration and hence the activation energy via zero-point energy changes. It was postulated that:³

(A) The change in hybridization of the reacting carbon atom (sp^3 initially, sp^2 in the transition state) produced zero-point energy changes in a direction which tended to make the heavy compound react more slowly.

(B) The relative positions of entering and leaving groups will affect the ease with which the α -C—H bonds may be bent. Where crowding of the C—H bond is pronounced, fundamental modes involving C—H deformations in an important way will have higher characteristic frequencies, and the resulting zero-point changes might exceed those from factor A. In consequence the net effect would then be a more rapid reaction of the heavy compound.

If the transition state of reaction is more crowded than the initial state, then deuteration might be expected to produce an increased rate of reaction as a consequence of dominance by factor B. Such a situation would prevail where a high degree of nucleophilic assistance was required for reaction, as with the methyl halides, and the expected decrease in effect is observed as the interaction by the entering group is decreased by "better" leaving groups. As we alter the alkyl grouping by alpha methylation, nucleophilic assistance becomes less necessary and the crowding in the transition state (factor B) fades out. Eventually, factor A gives rise to an isotope effect (k_H/k_D) greater than unity. For a given alkyl group, similar changes with reversal of effect may be seen as the X group is varied.

Deutero-*n*-propyl bromide reacts more quickly than its light analogue ($k_H/k_D = 0.98_0$) whereas *n*-propyl methanesulphonate reacts more slowly when deuterated ($k_H/k_D = 1.03_6$). Again this change in the deuterium isotope effect is attributed to a more crowded transition state in the bromide reaction where nucleophilic interaction is greater than in the methanesulphonate reaction. For other alkyl groups the changes are parallel; the alpha-deuterium isotope effect increases as the transition state becomes less crowded, e.g. the rate ratios k_H/k_D for ethyl iodide, bromide, and methanesulphonate are 0.95_6 , 0.98_3 , and 1.03_7 respectively. In addition to these effects there is a third which is a simple consequence of the mass alteration produced by isotopic substitution. The thermodynamic properties of the molecules depend on the masses of the constituent atoms so that independently of zero-point effects there may be a "thermodynamic" isotope effect. It is difficult to state in a general way exactly what the consequences of isotope substitution will be on the contributions to the thermodynamic parameters from the various degrees of freedom. Some obvious expressions were given in an earlier paper on the methyl compounds (2), but calculations for more complicated molecules are frequently difficult and often impossible because of lack of information. Some general comments can be made, however. For reactions such as these where two molecules become partially bonded on passing to the



³The suggestions concerning altered hybridization and modification of the effect by leaving group were first suggested by Streitwieser and co-workers (see ref. 8) and extended by us (ref. 2) to cover inverse isotope effects.

transition state, then the effect of substitution with a heavier isotope on the translational contribution will always be in a direction such that k_H/k_D tends to exceed unity. For α -deuteration, a substitution close to reaction site, the center of gravity of the molecule will be brought closer to the point at which mass increase from reaction occurs, and the rotational entropy of activation will accordingly decrease, i.e. k_H/k_D tends to exceed unity. It seems reasonable to neglect changes in the vibrational contribution in this context, by comparison with the zero-point energy changes which will arise from the same source. Detailed calculations have been made in cases where it has been practical (2, 5) and the general conclusion is that the "thermodynamic" effect favors slower reaction for the heavy compound and is of a magnitude which is comparable with observed effects in some cases, but cannot account for inverse isotope effects.

Further Considerations

Interpretation in terms of factor A, the hybridization change, and B, crowding by the entering group, seemed reasonably satisfactory and led to a self-consistent scheme for the α -deuterium kinetic isotope effects. There are some aspects of factor A, however, which seem doubtful: the intermediate in an S_N1 reaction will be the carbonium ion so that the transition state will probably not have completely altered hybridization of the reacting carbon, and the more the molecule can accommodate the developing charge by internal stabilization the nearer will be the configuration to tetrahedral in the transition state (6). In an S_N2 reaction, however, the hybridization change will probably be complete in the transition state with the entering and leaving groups interacting with the p orbital and the C—H bonds sp^2 hybridized (7). Thus hybridization change will be most marked in S_N2 reactions although zero-point effects will be modified by the presence of the entering group. It seems that the hybridization change is a necessary part of the reaction but is not necessarily responsible for the decrease in zero-point sum which plays such an important part in our considerations of the α -isotope effect. The difficulty in connection with this latter point is well illustrated by Streitwieser's comment on the effect of assuming different models for the sp^2 C—H bond (8). Making the usual reservations concerning the comparison of force constants we can find (9) wide overlapping ranges of force constants for sp^2 and sp^3 bonds. Some of the confusion is undoubtedly the consequence of the application of varying force fields in the spectral analysis but some consistency does appear when similar treatments are applied; for example Table II shows an increase in stretching

TABLE II
Effect of bond type on C—H force constant (13)

System	Bond	Constant $\times 10^{-8}$ dyne/cm
CH	p	4.09
CH ₄	sp^3	4.79
C ₂ H ₄	sp^2	5.1
C ₂ H ₂	sp	5.85

force constant with increased s character in the C—H bond, which contradicts the hypothesis A set up to explain the α -deuterium isotope effect.

The bending constants appear to change in the opposite direction. Using simple valence force fields, Linnett (10) quotes the bending constants given below. In contrast, using orbital valence force fields to analyze CH₄ spectra, C—H bond bending has a

TABLE III
 S.V.F.F. bending constants

System	Bending constant (erg/radian ² × 10 ¹¹)
$\text{C}-\text{C}\text{H}$	0.66
$\text{C}=\text{C}\text{H}$	0.60
$\text{C}\equiv\text{C}\text{H}$	0.24

constant 1.35×10^5 dyne/cm for doubly degenerate vibrations and 0.86×10^5 dyne/cm for triply degenerate vibrations whereas a comparable figure for ethylene is 0.95×10^5 and between 1.03 and 1.09×10^5 for formaldehyde, depending on the exact dimensions of the molecule which are taken in the analysis (10, 12). Thus the evidence that a hybridization change $sp^3 \rightarrow sp^2$ does produce the proposed zero-point change appears to be inconclusive. It is possible that the decrease in frequency springs from other sources, and one in particular seems worth considering.

Examination of vibrational spectra has shown that they may be satisfactorily accounted for by including potential energy terms for non-bonded atomic interactions comparable with those for intermolecular repulsions (10, 12-16). In molecules of the type XY_3 , XY_4 , XY_6 , non-bonded interactions must be taken into account when considering molecular distortions. CH_4 could be treated neglecting $\text{H} \dots \text{H}$ repulsion; it was assumed negligible in treatments of C_2H_4 and HCHO with some reservations, and it was found necessary to include $\text{H} \dots \text{O}$ and $\text{H} \dots \text{C}$ repulsion using a function $v = a/R^{12}$. Simanouti (17-19) has also successfully analyzed the vibrational spectra of numerous XABCD compounds using valence force field plus non-bonded interatomic repulsion terms of magnitude comparable to those used by Lennard-Jones to describe rare gas interatomic forces. Encouraging results have also attended correlations of molecular geometry with simple hard-sphere potential energy functions for non-bonded intramolecular interactions (20). In the reactions that we have studied, there is a movement of the X group away from the reaction center so that a reduction in intramolecular forces between this group and the α -hydrogen atoms might be expected. The magnitude of the change will depend on the increase in the $\text{H}(\alpha)-\text{X}$ distance and the degree of charge separation that has occurred, but will undoubtedly produce a significant decrease in the force field that governs vibrations involving the $\text{C}-\text{H}$ bonds. It is postulated, therefore, that the increased $\text{H}(\alpha)-\text{X}$ distance in the transition state produces a decrease in the zero-point sum as a consequence of reduced intramolecular van der Waals forces. This postulate is really an extension of factor B in the earlier argument and the α -isotope effect now appears to be governed largely by steric effects. Obviously it is difficult to separate this possibility from that of altered hybridization but the proposed consequences of the $sp^3 \rightarrow sp^2$ hybridization change are not evident, whereas a zero-point decrease seems inevitable when non-bonded atomic interactions are reduced.

On this basis of varying intramolecular van der Waals forces it appears that the α -isotope effect can still be interpreted as a measure of the crowding about the carbon

atom which forms the reaction center. For entering and leaving groups of comparable sizes in different reactions k_H/k_D is interpreted as a measure of the extent to which bond-making and bond-breaking have occurred, with smaller ratios indicating predominance of bond-making processes and larger ratios indicating bond-breaking. Thus the alternative postulate does not materially alter the conclusions which were drawn from the observed effects but appears to offer a more satisfactory explanation of some of the changes involved in their production than does the original postulate concerning altered hybridization (8). This is not to say that the hybridization change does not occur; on the contrary it forms a very vital part of ideas on the nature of these reactions, but does say that the zero-point decrease is not an immediate and obvious consequence of the change.

EXPERIMENTAL

Ethyl- ad_2 alcohol (minimum 98% isotopic purity) supplied by Merck and Co. Ltd. was converted to ethyl- $1d_2$ *p*-toluenesulphonate by the method of Tipson (21). The crude product was distilled under vacuum; m.p. 30.0° C (uncorrected). A comparison of the nuclear magnetic resonance (N.M.R.) spectrum of this compound with that of an undeuterated sample indicated that the alpha carbon atom was fully deuterated.

Ethyl- ad_2 bromide and ethyl- ad_2 iodide were prepared by heating, to 50° C under a vacuum, ethyl- ad_2 *p*-toluenesulphonate with a 3-mole excess of the appropriate potassium halide in the presence of a small amount of triethylene glycol. The ethyl halide evolved was collected in a trap cooled with liquid N_2 and redistilled at reduced pressure.

Ethyl- ad_2 methanesulphonate was made by shaking, at room temperature for ca. 100 hours, an equimolar solution of ethyl- ad_2 bromide and silver methanesulphonate in acetonitrile. The precipitated silver bromide was removed by filtration and the remaining solution evaporated to dryness at reduced pressure. The residue was extracted with anhydrous ether and, after removal of the ether, the product was distilled under a vacuum. It is considered extremely unlikely that any deuterium exchange could take place during the conversion of the deuterated alkyl *p*-toluenesulphonates to the corresponding alkyl halides and methanesulphonates, for the alkyl groups which we have studied (24). The kinetic purity of the compound was verified by the straight-line kinetic plots which were obtained in all cases. With the techniques which have been developed in this laboratory this test has repeatedly proved to be more sensitive than the normal methods of analysis.

The reduction of acetone with lithium aluminum deuteride (minimum 97.4% isotopic purity) yielded isopropyl- ad alcohol. The reaction was carried out by the standard method, modified by the use of diethylene glycol diethyl ether as solvent and diethylene glycol monobutyl ether as the reagent to decompose the complex aluminum compounds (22, 23). The crude isopropyl- ad alcohol, recovered from the reaction mixture by a simple distillation, was redistilled; boiling range 83.5–85.0° C, $n_D^{22.5} = 1.3762$ (lit. $n_D^{20} = 1.3773$). The N.M.R. spectrum indicated that the alpha carbon atom was fully deuterated.

Isopropyl- ad *p*-toluenesulphonate, bromide, iodide, and methanesulphonate were prepared by a series of reactions analogous to that employed for the ethyl compounds.

n-Propyl- ad_2 bromide (minimum 98% isotopic purity) was purchased from Merck and Co. Ltd. The N.M.R. spectrum showed that the alpha carbon atom was ca. 90% deuterated. This bromide was converted into *n*-propyl- ad_2 benzenesulphonate and methanesulphonate by the silver sulphonate method as described for the ethyl compounds. The iodide was prepared from the benzenesulphonate and potassium iodide.

For each of the above preparations a parallel reaction was carried out with undeuterated compounds. The products were used to check the rate constants of the protium compounds which had been determined in the course of previous work under the same conditions. Good agreement was obtained in all cases.

ACKNOWLEDGMENTS

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ISOLATION AND PROPERTIES OF A GLUCOMANNAN FROM THE WOOD OF RED MAPLE (*ACER RUBRUM* L.)¹

A. JABBAR MIAN AND T. E. TIMELL

ABSTRACT

A glucomannan has been isolated from the wood of red maple (*Acer rubrum* L.) in a yield corresponding to 92% of the mannose residues in this wood and with a ratio of mannose to glucose of 2:1. Partial hydrolysis of the polysaccharide yielded 4-*O*- β -D-mannopyranosyl-D-mannose, 4-*O*- β -D-mannopyranosyl-D-glucose, 4-*O*- β -D-glucopyranosyl-D-mannose, 4-*O*- β -D-glucopyranosyl-D-glucose, and *O*- β -D-mannopyranosyl-(1 \rightarrow 4)-*O*- β -D-mannopyranosyl-(1 \rightarrow 4)-D-mannose. The methylated glucomannan on hydrolysis gave a mixture of di-*O*-methylhexoses, 2,3,6-tri-*O*-methyl-D-mannose, 2,3,6-tri-*O*-methyl-D-glucose, and 2,3,4,6-tetra-*O*-methyl-D-glucose in a mole ratio of 7:29:13:1. The methylated polysaccharide contained 55 hexose residues per average molecule, while the corresponding value for the nitrate derivative was 67. It is concluded that the glucomannan is composed of a minimum of 70 glucose and mannose residues linked together by (1 \rightarrow 4)- β -glycosidic bonds to linear molecules. The glucose residues are probably interposed between two or three contiguous mannose residues.

In the last few years, glucomannans have been isolated from the wood of many gymnosperms, where this polysaccharide constitutes the preponderant hemicellulose. Little attention has so far been directed towards the origin of the relatively few mannose residues present in the wood of the arborescent angiosperms. A glucomannan has been isolated from trembling aspen (1) and similar polysaccharides have been obtained also from red alder and from madrona (2). The isolation of a glucomannan from white birch was recently reported (3). This paper is concerned with the isolation of a glucomannan from red maple (*Acer rubrum* L.) and with the properties of this diheteroglycan.

RESULTS AND DISCUSSION

Red maple wood, containing 2.4% mannose residues, was delignified with acid chlorite (4) to give a holocellulose in a yield closely corresponding to the lignin content of the wood. The holocellulose was exhaustively extracted with 24% potassium hydroxide, which removed a pure methylglucuronoxylan. Subsequent extraction with sodium hydroxide - borate (5, 6) gave a mixture containing mannose and glucose residues in a ratio of 1.34:1 in addition to 14% of xylose. One treatment with barium hydroxide (7) removed the xylose containing polysaccharide and increased the above ratio to 1.94:1. The crude and purified products contained 95% and 92%, respectively, of the mannose residues originally present in the wood.

The pure glucomannan, $[\alpha]_D -31^\circ$, was a white powder, insoluble in water. When oxidized with periodate, it consumed 1.0 mole of oxidant per hexose residue. The number-average molecular weight of the nitrate derivative as determined by osmometry (8) was 18,200, corresponding to a degree of polymerization of 67. Boundary electrophoresis according to Tiselius (9) indicated that the polysaccharide was chemically homogeneous.

A portion of the glucomannan was partially hydrolyzed with aqueous formic acid to give a mixture of sugars which was resolved on a charcoal-Celite (10) column by gradient (11) elution with aqueous ethanol (12). The sugars obtained included D-mannose, 4-*O*- β -D-mannopyranosyl-D-mannose, 4-*O*- β -D-mannopyranosyl-D-glucose, 4-*O*- β -D-glucopyranosyl-D-mannose, 4-*O*- β -D-glucopyranosyl-D-glucose, and *O*- β -D-mannopyranosyl-(1 \rightarrow 4)-*O*- β -D-mannopyranosyl-(1 \rightarrow 4)-D-mannose. Mannobiose and glucosyl mannose

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Contribution from the Pulp and Paper Research Institute of Canada and the Department of Chemistry, McGill University, Montreal, Que.

were isolated in the highest, cellobiose in the lowest, yield. Two tetraose compounds were also obtained crystalline, containing both glucose and mannose residues.

Another portion of the glucomannan was methylated to completion and subsequently hydrolyzed to a mixture of sugars which was resolved on a charcoal-Celite column. A mixture of di-*O*-methylhexoses, 2,3,6-tri-*O*-methyl-D-mannose, 2,3,6-tri-*O*-methyl-D-glucose, and 2,3,4,6-tetra-*O*-methyl-D-glucose was obtained in a mole ratio of 7:29:13:1. The tri-*O*-methylmannose was identified through its characteristic 1,4-di-*p*-nitrobenzoate derivative (13) and the tri- and tetra-*O*-methylglucoses crystallized. The methylated glucomannan contained 55 hexose residues per average molecule as estimated by osmometry.

From the above evidence a tentative structure can now be assigned to the glucomannan present in red maple wood. The large quantity of 2,3,6-tri-*O*-methylhexoses shows that the polysaccharide is composed of (1 \rightarrow 4)-linked hexose residues and this conclusion is corroborated by the consumption of 1 mole of periodate per hexose residue. The negative rotation of the glucomannan suggests that the linkage is of the β -type. The isolation of 2,3,4,6-tetra-*O*-methyl-D-glucose indicates that most of the non-reducing end groups consist of glucose residues, one such end group being present per 50 anhydrohexose units. Since the average molecule contained 55 hexose residues, the glucomannan contained few, if any, branching points. The occurrence of the di-*O*-methylhexoses was probably due to demethylation during methanolysis and hydrolysis.

The above conclusions were corroborated by the nature of the oligosaccharides formed on partial hydrolysis of the glucomannan. The high yield of mannobiose and mannotriose as compared to the low yield of cellobiose suggests that few of the glucose residues were contiguous. Relatively more glucosyl mannose and more mannosyl glucose were isolated than have previously been obtained from softwood glucomannans (14-16). This is to be expected in view of the lower ratio of mannose to glucose in hardwood as compared with softwood glucomannans. Similarly, mannose has been found to form most of the non-reducing end groups in glucomannans from gymnosperms (16-21), while both the present glucomannan and a similar polysaccharide from white birch wood (22) seem to contain more glucose than mannose end groups.

The glucomannan contained approximately 70 hexose residues per average molecule. This value might not represent the molecular magnitude of the native polymer since acid chlorite was used to delignify the wood (23).

The present polysaccharide is the first representative hardwood glucomannan whose structure has been determined in detail, and direct comparison with other glucomannans of similar origin is therefore not possible. Methylation studies of the glucomannan previously isolated from aspen wood (1) indicated the presence of a (1 \rightarrow 4)-linked polysaccharide with a ratio between glucose and mannose of 1:2. A glucomannan from western red alder (2) has been reported to contain glucose and mannose in a ratio of 1:1.5. For a birch glucomannan (3) this ratio was 1:1.1. Subsequent investigations of other hardwood glucomannans (24) have shown that while the ratio of mannose to glucose is close to 1.0 for birches, most other hardwoods exhibit a ratio of 1.5-2.

Glucomannans from gymnosperms usually contain approximately three times as many mannose as glucose residues. The glucomannans present in arborescent angiosperms appear to have a higher relative content of anhydroglucose units. Apart from this discrepancy, there seem to be few differences between hardwood and softwood glucomannans. Both types of polysaccharides consist of essentially linear macromolecules composed of 100-200 (1 \rightarrow 4)-linked β -D-hexose residues, probably with many of the glucose residues interposed as single units between several contiguous mannose residues. Relative sugar

composition and relative abundance are therefore the only two respects in which softwood and hardwood glucomannans differ in any essential way.

EXPERIMENTAL

All specific rotations are equilibrium values unless otherwise stated and were determined at 20° C. Melting points are corrected. Evaporations were carried out *in vacuo* at 40–50° C.

Paper Chromatography

Solvent systems used for separating sugars were (v/v): (A) ethyl acetate – acetic acid – water (9:2:2), (B) butan-1-ol–pyridine–water (10:3:3), and (C) butanone–water (89:11). Whatman No. 1 filter paper and the descending technique were used. Paper electrophoresis was carried out with Whatman No. 3 MM filter paper in 0.05 *M* borate buffer at 750 volts. The spray reagent was *o*-aminodiphenyl (25).

Wood

Logs from a freshly cut red maple were barked, chipped, and converted to sawdust. The 20–80 mesh fractions were exhaustively extracted with ethanol–benzene (1:2 v/v), extracted with cold water, and dried in the air. The following data were obtained by standard analytical procedures: cellulose (44.1%), lignin (24.0%), ash (0.2%), acetyl (3.8%), uronic anhydride (3.5%), residues of galactose (0.6%), glucose (46.6%), mannose (2.4%), arabinose (0.5%), and xylose (14.8%).

Isolation of a Crude Glucomannan

Extractive-free wood meal (1080 g) was suspended with stirring in water (18 liters) at 70–80° C. Acetic acid (120 ml) and sodium chlorite (360 g) were added every hour for a total period of 7 hours (4). The reaction mixture was cooled, and the solids were washed by decantation with tap water. They were then transferred to a filter and washed with distilled water and ethanol. The white product was dried in the air to yield 840 g of holocellulose, 76% of the wood.

The holocellulose (840 g) was shaken in an atmosphere of nitrogen with 24% (w/w) aqueous potassium hydroxide (6 liters) at room temperature for 3 hours. The alkaline extract was removed by filtration through fritted glass and the residue was washed with water. The still wet residue was extracted in the same way with 17.5% sodium hydroxide to which 4% boric acid had been added (5, 6). The alkaline extracts and washings (8 liters) were poured into ethanol (30 liters) containing glacial acetic acid (3 liters). The precipitate formed was washed on the centrifuge with 80% aqueous ethanol, ethanol, and petroleum ether (b.p. 30–60° C), yielding a white powder (40.0 g). Sugar residues in the potassium hydroxide extract were xylose and uronic acids, in the alpha-cellulose (unextracted residue) glucose and traces of xylose. The alkaline borate extract (the crude glucomannan) contained mannose and glucose in a ratio of 1.31:1 and 14% xylose residues.

Purification of the Crude Glucomannan

Crude glucomannan (40 g) was dissolved in 10% sodium hydroxide (1 liter) and 5% aqueous barium hydroxide (2 liters) was added with constant stirring over a period of 2 hours. The precipitate formed was collected by centrifuging, washed twice with water, acidified with acetic acid, and poured into ethanol (5 liters). The precipitate was recovered in the usual way (35 g, 3.3% of the wood). Mannose/glucose: 1.94. Xylose: nil. $[\alpha]_D^{25} -31^\circ$ (c, 1.0 in 10% sodium hydroxide).

Partial Hydrolysis of the Glucomannan

Glucomannan (9.7 g) was dissolved in 90% formic acid (50 ml). Water (50 ml) was added and the solution was heated to 95–97° C for 3 hours (14). After cooling, the clear solution was removed by decantation and the solid residue was again hydrolyzed. This treatment was repeated twice. The solutions were combined and the formic acid was removed by evaporation with water. Formate esters were hydrolyzed with 0.5 *N* sulphuric acid at 100° for 10 minutes (100 ml). After neutralization with barium carbonate, filtration through Celite, and treatment with Amberlite IR-120 exchange resin, evaporation gave a clear sirup (7.5 g). Paper chromatography (solvents A and B) indicated the presence of hexoses and hexose oligosaccharides.

Resolution of the Hydrolyzate

The partial hydrolyzate (7.5 g) was dissolved in water (50 ml) and added to the top of a Darco G-60 – Celite column (10) (6×64 cm). Gradient elution (11) was carried out with 3 liters each of the following solvents: 2% aqueous ethanol → 10% ethanol, 10% ethanol → 20% ethanol, and 20% ethanol → 40% ethanol. Fractions, 25 ml each, were collected at an average rate of two per hour and the sugar content of every third fraction was estimated by paper chromatography (solvent B).

Identification of Sugars

All sugars moved on the paper chromatogram (solvents A and B) at the same rate as authentic specimens.

(1) Monosaccharides

Following a mixture of glucose and mannose with a trace of xylose (1.45 g), pure D-mannose (1.82 g) was eluted from the column, m.p. and mixed m.p. 132° C, $[\alpha]_D +12.8^\circ$ (*c*, 2.3 in water). The mannose phenylhydrazone had a melting point and mixed melting point of 194° C.

(2) 4-O-β-D-Mannopyranosyl-D-mannose

Hydrolysis of this compound (790 mg) gave only mannose. The mannobiose, after recrystallization from methanol, had a melting point and mixed melting point of 200–201° C, $[\alpha]_D -8.5^\circ$ (*c*, 1.0 in water).

(3) 4-O-β-D-Mannopyranosyl-D-glucose

Hydrolysis of this fraction (193 mg) gave equal amounts of mannose and glucose. After reduction with sodium borohydride, mannose only was obtained on hydrolysis. The compound, $[\alpha]_D +27^\circ$ (*c*, 1.5 in water), could not be induced to crystallize, nor could the derived octaacetate derivative be obtained in crystalline form.

(4) O-β-D-Mannopyranosyl-(1 → 4)-O-β-D-mannopyranosyl-(1 → 4)-D-mannose

This fraction (171 mg) readily crystallized from methanol containing some water and butan-1-ol, m.p. and mixed m.p. 230–232° C, $[\alpha]_D -25^\circ$ (*c*, 1.3 in water). Partial hydrolysis followed by examination by paper chromatography suggested the presence of unchanged mannotriose, mannobiose, and mannose. Complete hydrolysis gave mannose.

(5) 4-O-β-D-Glucopyranosyl-D-glucose

This disaccharide (30 mg) on recrystallization from aqueous methanol had melting point and mixed melting point 226–227° C, $[\alpha]_D +24^\circ$ (*c*, 1.0 in water). Complete hydrolysis gave only glucose.

(6) *4-O- β -D-Glucopyranosyl-D-mannose*

The disaccharide (663 mg) on hydrolysis gave equal amounts of glucose and mannose. The compound, when recrystallized from ethanol, had melting point and mixed melting point 137–138° C, $[\alpha]_D +11^\circ \rightarrow +6^\circ$ (*c*, 1.0 in water).

(7) *Hexotetraose Fraction*

This fraction (23 mg) had a melting point of 237–238° C. Partial hydrolysis with formic acid gave glucosyl mannose, glucose, and mannose. The degree of polymerization was estimated as 4.1 (26).

(8) *Hexotetraose Fraction*

This compound had a melting point of 210–212° C (20 mg). Partial hydrolysis yielded a hexotriose, glucosyl mannose, glucose, and mannose. The degree of polymerization was 4.2 (26).

Methylation of the Glucomannan

Glucomannan (13 g) was dissolved in 40% (w/w) aqueous sodium hydroxide in an atmosphere of nitrogen and dimethyl sulphate (250 ml) was added dropwise over a period of 48 hours. This process was repeated three times. Solid sodium hydroxide (200 g) was added, followed by dimethyl sulphate (250 ml). This treatment was repeated six times, water being added whenever necessary for efficient stirring. The reaction mixture was neutralized with sulphuric acid to pH 4 and then heated to boiling. The precipitated polysaccharide was recovered by filtration and washed briefly with hot water. Yield, 7.5 g; OCH_3 , 44.3%.

The material (7.0 g) was dissolved in dry dimethyl formamide (150 ml) (27) and treated with methyl iodide (50 ml) and silver oxide (50 g) for 48 hours at room temperature. The polysaccharide was recovered in the usual way (27) to yield 4.9 g of material. The infrared diagram indicated the absence of hydroxyl groups.

Hydrolysis of the Methylated Glucomannan and Resolution of the Hydrolyzate

Methylated glucomannan (3.5 g) was boiled under reflux with 0.7 *N* methanolic hydrogen chloride for 7 hours and subsequently with *N* hydrochloric acid for 7 hours. The solution was neutralized with silver carbonate, filtered through Celite, treated with hydrogen sulphide, again filtered through Celite, and finally evaporated to give a clear sirup (3.1 g). Paper chromatography (solvent C) indicated the presence of di-, tri-, and tetra-*O*-methylhexoses.

The hydrolyzate (3.0 g) was added to the top of a column (5×56 cm) containing a 1:1 mixture of Darco G-60 charcoal and Celite. Gradient elution was effected with 3 liters each of the following solvents: 5% aqueous ethanol \rightarrow 10% ethanol, 10% ethanol \rightarrow 30% ethanol, and 30% ethanol \rightarrow 60% ethanol. The resolution was followed by paper chromatography (solvent C) and, for the tri-*O*-methylhexoses, by measuring the optical rotation of the fractions.

(1) *Di-O-methylhexoses*

This fraction (290 mg) on demethylation with hydrobromic acid (28) gave glucose and mannose on the paper chromatogram.

(2) *2,3,6-Tri-O-methyl-D-mannose*

The sirup (1355 mg), $[\alpha]_D -12.5^\circ$ (*c*, 1.2 in water), was converted to the characteristic di-*p*-nitrobenzoate derivative (13), m.p. and mixed m.p. 186–187° C after recrystallization from ethyl acetate, $[\alpha]_D +33^\circ$ (*c*, 0.5 in chloroform).

(3) 2,3,6-Tri-O-methyl-D-glucose

This compound (640 mg), $[\alpha]_D +41^\circ$ (*c*, 1.3 in water), could not be induced to crystallize. The 2,3,6-tri-O-methyl-D-glucose-1,4-di-*p*-nitrobenzoate (13) had melting point and mixed melting point 190°C , $[\alpha]_D -33^\circ$ (*c*, 0.6 in chloroform).

2,3,4,6-Tetra-O-methyl-D-glucose

The last fraction (51 mg), on standing, crystallized. Recrystallization from hot petroleum ether gave melting point and mixed melting point $89-90^\circ\text{C}$. A portion of the original sirup on demethylation (28) yielded glucose and a trace of mannose. The fraction was thus mainly 2,3,4,6-tetra-O-methyl-D-glucose.

Periodate Oxidation of the Glucmannan

The glucmannan (150–200 mg) was oxidized in the dark for various lengths of time with 50.0 ml of 0.05 *M* sodium metaperiodate. Consumption of oxidant was measured by the excess arsenite method. Extrapolation to zero time indicated a consumption of periodate of 1.0 mole per hexose residue.

Determination of Number-Average Molecular Weights

The glucmannan was converted to its nitrate ester as described previously (30, 31). Osmotic pressure measurements were carried out as reported elsewhere (16, 29). The solvent for the methylated glucmannan was a 9:1 (v/v) mixture of chloroform and ethanol, and for the nitrate derivative *n*-butyl acetate. The experimental results are presented in Table I. Number-average molecular weights (\bar{M}_n) were calculated from the relationship $\bar{M}_n = 25,700/(h/w)_{w=0}$.

TABLE I
Osmometry data

Methylated glucmannan			Nitrated glucmannan		
<i>w</i> *	<i>h</i> †	<i>h/w</i>	<i>w</i>	<i>h</i>	<i>h/w</i>
2.464	5.791	2.350	3.368	5.077	1.508
1.896	4.375	2.307	3.356	4.900	1.460
1.662	4.030	2.425	2.262	3.206	1.417
1.020	2.385	2.338	1.124	1.625	1.445
0	—	2.32	0	—	1.41

*Concentration in grams/kilogram of solution.

†Osmotic height in centimeters of solution.

Boundary Electrophoresis

The glucmannan was dissolved to a concentration of 1–2% in a buffer solution containing 7.50 g of boric acid and 4.0 g of sodium hydroxide per liter (30). The instrument was a Spinco Model H apparatus. Only one maximum was observed at various intervals of time, in addition to a stationary salt boundary.

ACKNOWLEDGMENT

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PROTONATION OF THE AMIDE GROUP

I. THE BASICITIES OF SUBSTITUTED BENZAMIDES¹

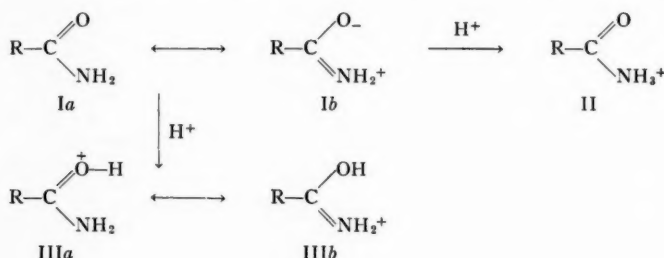
J. T. EDWARD,² H. S. CHANG,² K. YATES,³ AND ROSS STEWART³

ABSTRACT

The basicities of benzamide and of 11 meta- and para-substituted benzamides in sulphuric acid media have been determined by a spectrophotometric method. The pK_{BH^+} values of the protonated benzamides were found to be proportional to the Hammett σ constants for the substituents, unlike the pK_{BH^+} values of the protonated benzaldehydes, acetophenones, and benzoic acids, which are approximately proportional to σ^+ constants. The lack of conjugation between the protonated amide group and the ring, which is indicated by these results, is most easily interpreted in terms of N-protonation although O-protonation cannot be completely excluded. Various other aspects of the problem of N- versus O-protonation are also discussed.

INTRODUCTION

While it has been known for a long time that amides behave as moderately strong Brønsted bases in mineral acids (1), taking up one proton (2, 3), the structure of the ion formed is still debated. Two alternative sites are available for attachment of the proton, the amino nitrogen or the carbonyl oxygen. In 1931 Hantzsch (4) presented evidence for the O-protonated form (III; R = Ph) for benzamide (I; R = Ph) in concentrated



sulphuric acid, by noting the similarity of the ultraviolet absorption spectrum of this solution with that of ethyl benzimidate in acid. The protonated form of the latter compound can only have the structure $\text{Ph}-\text{C}(\text{OEt})=\text{NH}_2^+$. The later work of Mizushima *et al.*, who studied the ultraviolet absorption of N-methylacetamide in acid, appeared to indicate N-protonation (5), but has not been confirmed (6).

Huisgen and Brade (7) presented arguments in favor of O-protonation based on the orders of basicities of substituted amides. However, their arguments involve several questionable assumptions and cannot be considered conclusive. Further evidence for O-protonation has come from studies of amides in neutral and in acid solution by nuclear magnetic resonance (8, 9, 10, 11, 12). In neutral solution it can be shown that there is a barrier to rotation about the C-N linkage, presumably because of its partial double bond character due to the resonance ($\text{Ia} \leftrightarrow \text{Ib}$). A barrier to rotation is found also for

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Contribution from the Departments of Chemistry, McGill University, Montreal, Que., and the University of British Columbia, Vancouver, B.C.

²McGill University, Montreal, Que.

³University of British Columbia, Vancouver, B.C.

amides in strong acid, as would be expected for the O-protonated form ($\text{IIIa} \leftrightarrow \text{IIIb}$), but not for the N-protonated form (II). However, in moderate concentrations of acid, nuclear magnetic resonance (n.m.r.) studies indicate that some N-protonation also occurs, although it has been considered that probably O-protonation predominates (11). This interpretation of the n.m.r. results has been criticized by Spinner (13), who has suggested that they are more in accord with N-protonation.

On theoretical grounds, it has been generally considered (14, 15) that the O-protonated form (III) should be preferred over the N-protonated form (II) because it preserves the resonance stabilization ($\text{IIIa} \leftrightarrow \text{IIIb}$) characteristic of the amide molecule itself ($\text{Ia} \leftrightarrow \text{Ib}$). Spinner, who has supported the concept of N-protonation (16), has taken the view that π electrons are not delocalized in conjugated systems (17). This idea, which will be unacceptable to many, should not be considered central to the problem. Undoubtedly, ion III possesses much more resonance energy than does ion II. The latter's total energy, however, may still be the lower of the two.

Evidence favoring N-protonation exists in the observed decreases in the N—H and increases in the C=O stretching frequencies in the infrared and Raman region (5, 16, 18, 19, 20). Particularly significant has been the evidence for an N-protonated structure for the urea cation (18), since it has been considered that for this ion the O-protonated structure is, even more than for amide conjugate acids, favored by the possibilities for resonance stabilization (15).*

It is apparent that further evidence on the structure of protonated amides is desirable. In the present paper we report the effect of meta- and para-substitution on the $\text{p}K_{\text{BH}^+}$ of benzamide. If protonation takes place on the nitrogen, no direct resonance interaction between the charged center and the substituent is possible, and it should be expected that the $\text{p}K_{\text{BH}^+}$ values should be proportional to σ , Hammett's constant for the substituent (22). On the other hand, if protonation takes place on the oxygen, then (as in the case of substituted acetophenones (23) and benzaldehydes (24)) direct resonance interaction is possible between the substituent and the charged carbonyl group, and one would expect $\text{p}K_{\text{BH}^+}$ to be proportional to σ^+ (25, 26) or at least to deviate from a linear σ relation. This method has been used to show that carbonyl oxygen protonation occurs in the case of the carboxyl group since the $\text{p}K_{\text{BH}^+}$ values are approximately proportional to σ^+ (27).

EXPERIMENTAL

Materials

N-Methyl- and N,N-dimethylbenzamide were prepared by the method of Galat and Elion (28) from benzamide and methylamine hydrochloride and from benzamide and dimethylamine hydrochloride respectively. The other amides were commercial products, or were prepared by standard methods from the acids or acid chlorides. N,N-Dimethylbenzamide was obtained as a liquid, b.p. $135^\circ\text{--}137^\circ\text{C}$ at 16 mm (lit. b.p. $132^\circ\text{--}133^\circ\text{C}$ at 15 mm (29)); its ultraviolet spectrum in water was identical with that found by Ley and Specker (30). The other amides were solids, and were recrystallized from alcohol to constant melting point, which in all cases was close to values reported in the literature. Sulphuric acid of various concentrations was prepared and standardized following methods already described (23, 24).

*The validity of the identification of the carbonyl stretching band in these salts is currently being tested with the use of oxygen-18 labelled compounds (21).

Procedure

Absorption spectra of the benzamides in water and in various concentrations of sulphuric acid were measured at $25 \pm 0.1^\circ$ according to published methods (23, 24). Solutions in water and in 59–69% acid (see Table I) were used to locate the wavelengths of

TABLE I
Absorption spectra of substituted benzamides and acetophenones

Substituent	Benzamides				Acetophenones† in 44.0% H ₂ SO ₄	
	In water		In 59.0% H ₂ SO ₄ *		λ_{max} (m μ)	ϵ_{max}
	λ_{max} (m μ)	ϵ_{max}	λ_{max} (m μ)	ϵ_{max}		
Hydrogen	225	9100	245 (a)	11950	250	11500
<i>m</i> -Methyl	231	9770	250	11500	252	7590
<i>p</i> -Methyl	238	11500	258 (b)	14400	260	
<i>m</i> -Methoxy	(231)‡	7240	251	8510	253	8910
<i>p</i> -Methoxy	253	14800	282	16900	282	13800
<i>m</i> -Chloro	(229)‡	7460	245 (c)	9530	248	8920
<i>p</i> -Chloro	237	12600	256	14800	258	15000
<i>m</i> -Bromo	(232)‡	8130	247	10000	248	8710
<i>p</i> -Bromo	242	13500	261	15500	270	
<i>p</i> -Fluoro	229	8860	248 (c)	11960	250	10980
<i>m</i> -Nitro	215	20600	229 (d)	21100	232	17000
<i>p</i> -Nitro	266	11200	264 (e)	14460	270	13500
<i>N</i> -Methyl	(226)‡	10000	242	12000		
<i>N,N</i> -Dimethyl	218	7250	236	8320		

*Except in the following instances: (a) 59.3% H₂SO₄, (b) 57.2% H₂SO₄, (c) 60.0% H₂SO₄, (d) 64.0% H₂SO₄, (e) 69.7% H₂SO₄.

†Ref. 23.

‡Shoulder.

maximal absorption of the unprotonated (λ_u) and protonated (λ_i) forms respectively. Distinct maxima were obtained in all cases except for the unionized forms of *m*-chloro- (Fig. 1), *m*-bromo-, *m*-methoxy-, and *N*-methyl-benzamide, which showed only shoulders on the sides of more intense peaks situated in the vacuum ultraviolet region. In these cases readings of the absorption of the unionized form were taken at several wavelengths in the vicinity of the shoulder, and those wavelengths chosen to represent λ_u which resulted in the smoothest plots of $\epsilon(\lambda_i) - \epsilon(\lambda_u)$ against H_0 .

2-Furamide in water had λ_{max} 253 m μ , ϵ_{max} 12,400, and in 59.0% H₂SO₄ λ_{max} 275 m μ , ϵ_{max} 14,900, and was investigated in the same way as the benzamides.

Hydrolysis of the amides was shown to be negligible in the time required for measurements by periodic checks of the measurements of absorption in the acidity range known to give maximal rates of hydrolysis (31). After several hours standing these showed variations of less than 2%.

Calculation of pK_{BH^+} Values

The pK_{BH^+} values were determined by the graphical method of Davis and Geissman (32) as used previously by Stewart and Yates (23, 24), and are listed in Table II for the benzamides; 2-furamide had a pK_{BH^+} of -2.61 . *m*-Nitrobenzamide in water showed two well-defined absorption peaks (Fig. 2), and two pK_{BH^+} values were obtained depending on the wavelength chosen for $\epsilon(\lambda_u)$. In the absence of medium effects these values should be identical; the difference between them is a measure of the precision of the

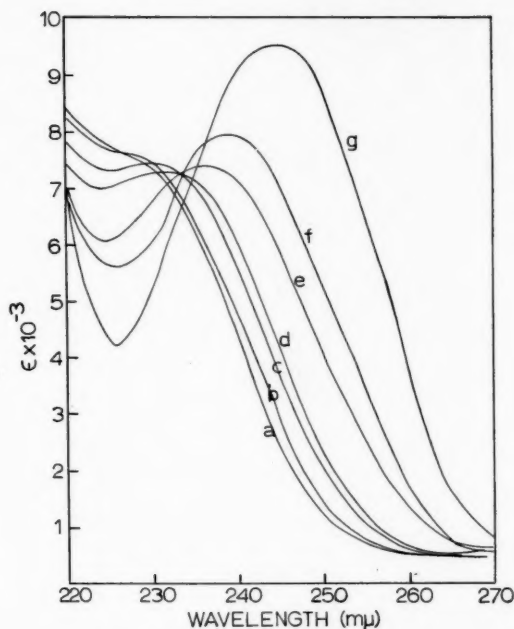


FIG. 1. Absorption spectra of *m*-chlorobenzamide in the following concentrations of aqueous sulphuric acid: a, 0%; b, 12.8%; c, 26.9%; d, 31.2%; e, 41.0%; f, 46.4%; g, 60.0%.

TABLE II
p*K*_{BH⁺} values of substituted benzamides

Substituent	-p <i>K</i> _{BH⁺}	Substituent constants*	
		σ	σ ⁺
Hydrogen	2.16	0	0
<i>m</i> -Methyl	2.15	-0.069	-0.066
<i>p</i> -Methyl	2.01	-0.170	-0.311
<i>m</i> -Methoxy	2.35	0.115	0.047
<i>p</i> -Methoxy	1.80	-0.268	-0.778
<i>m</i> -Chloro	2.59	0.373	0.399
<i>p</i> -Chloro	2.47	0.227	0.114
<i>m</i> -Bromo	2.75	0.391	0.405
<i>p</i> -Bromo	2.47	0.232	0.150
<i>p</i> -Fluoro	2.24	0.062	-0.073
<i>m</i> -Nitro	2.99 (a)† 3.14 (b)†	0.710	0.674
<i>p</i> -Nitro	3.23	0.778	0.790
<i>N</i> -Methyl	2.13		
<i>N,N</i> -Dimethyl	1.62		

*Refs. 25, 26, and 33.

†(a) From plots of $\epsilon_{250} - \epsilon_{230}$ against H_0 . (b) From plots of $\epsilon_{225} - \epsilon_{220}$ against H_0 .

results. The basicities determined for benzamide and for *p*-methoxybenzamide differ slightly from values previously reported (31), probably in part because of the different graphical method used in analyzing the earlier results.

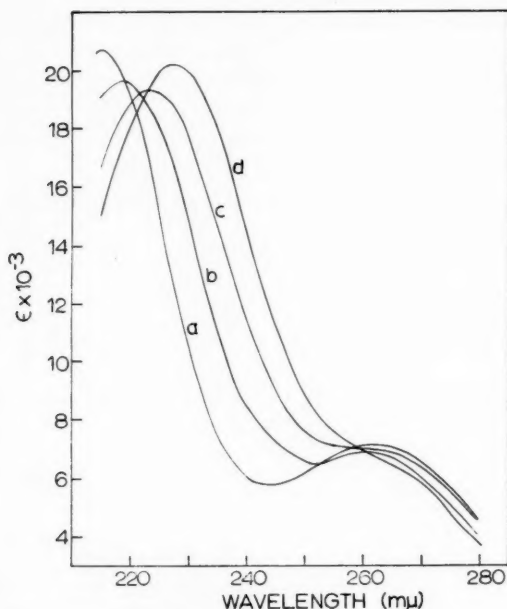


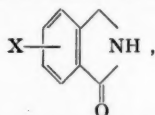
FIG. 2. Absorption spectra of *m*-nitrobenzamide in the following concentrations of aqueous sulphuric acid: a, 0%; b, 41.0%; c, 56.8%; d, 60.0%.

RESULTS AND DISCUSSION

The Basicities of Meta- and Para-Substituted Benzamides

In Figs. 3 and 4 the pK_{BH^+} values of the substituted benzamides are plotted against σ and σ^+ respectively (33). It can be seen that in the first case a good linear relationship is obtained ($r = 0.988$) with the usual precision (34) found for this type of ionization. The value of ρ (by the method of least squares) is 1.30. The correlation of pK_{BH^+} with σ^+ (Fig. 4) is much poorer ($r = 0.958$). The straight line has been drawn with respect to the groups *m*-methyl, *m*-bromo, and hydrogen, since the σ and σ^+ values of these groups are very close. In this case a large deviation is observed for *p*-methoxy, which is able to supply electrons by resonance to the carbonyl group. A correlation with σ^+ can only be attributed to O-protonation. A correlation with σ tells us that para substituents are not in conjugation with the protonated amide group. The most attractive explanation for this is that N-protonation has occurred. It is conceivable, however, that O-protonation has taken place and the lack of conjugation is due to lack of planarity between the ring and the protonated amide group. In other words, the extra resonance stabilization provided by the ring and its substituents might not be sufficient to cause coplanarity.*

*An attempt has been made to eliminate this possibility by examining the phthalimidine series,



in which coplanarity is enforced. However, the precision in measuring the basicities of phthalimidine ($pK_{BH^+} = -2.1$) and its 6-nitro derivating ($pK_{BH^+} \approx -3.1$) was found to be lower than for the benzamides and further work was not considered worth while (35).

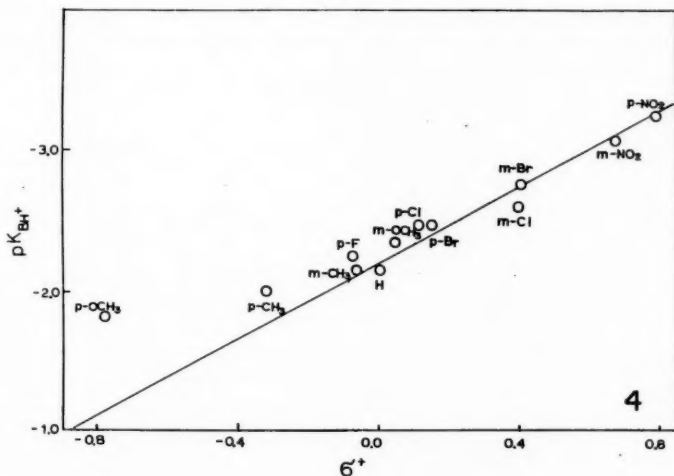
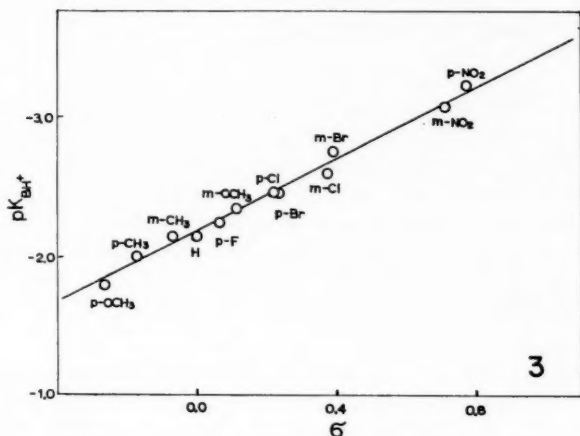


FIG. 3. pK_{BH^+} for substituted benzamides plotted against Hammett's σ constants.

FIG. 4. pK_{BH^+} for substituted benzamides plotted against Brown's σ^+ constants.

The Basicity of Furoamide

Furoic acid is a stronger acid ($pK_{HA} = +3.18$) than benzoic acid ($pK_{HA} = +4.20$) (22), the net electron pull due to the inductive and resonance polar effects (36) of the furyl group evidently being greater than that of the phenyl group. This effect would be expected to make furoamide a weaker base than benzamide, as is observed, if protonation takes place on the nitrogen and hence only inductive and resonance polar effects operate. In fact, we find that 2-furoamide ($pK_{BH^+} = -2.61$) is a considerably weaker base than benzamide ($pK_{BH^+} = -2.15$). On the other hand, if protonation took place on the carbonyl oxygen the direct resonance interaction possible between the ring oxygen and the protonated carbonyl group ($IVa \leftrightarrow IVb$) would be expected to make furoamide the stronger base.



It turns out, in fact, that resonance of this type is not as important as we had expected it to be. This follows from the fact that 2-furoic acid and benzoic acid, both of which, one can assume, protonate at the carbonyl oxygen (27), actually have similar basicities, -7.3 for 2-furoic acid (35) and -7.2 for benzoic acid (27). It appears that the resonance effect is only large enough to cancel approximately the inductive and resonance polar effects. Thus the support for the N-protonated form provided by the furamide basicity cannot be considered unequivocal.

Ultraviolet Spectra of Protonated Benzamides

A comparison of the spectral characteristics of protonated benzamides with those of similarly substituted unprotonated acetophenones in 44.0% sulphuric acid (Table I) shows them to be closely similar, the positions of the absorption maxima in most cases being within 2–3 $m\mu$ of each other. The similarity extends to the general shape of the absorption curves, as shown for acetophenone and protonated benzamide in Fig. 5.

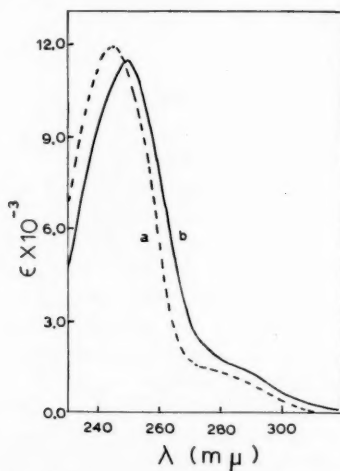


FIG. 5. Absorption spectra of benzamide in 59.3% sulphuric acid (a) and of acetophenone in 50% sulphuric acid (b). (Latter curve plotted from values from Flexser, Hammett, and Dingwall, *J. Am. Chem. Soc.* **57**, 2103 (1935).)

The same is true for protonated furamide (in 59.0% H_2SO_4 : λ_{max} 275 $m\mu$, ϵ_{max} 14,900), which closely resembles methyl 2-furyl ketone (in H_2O : λ_{max} 275 $m\mu$, ϵ_{max} 13,900 (37)).

These results are to be expected for the N-protonated structures, since it has been observed that replacement of a methyl by an $-\text{NH}_3^+$ group has only a minor effect on the ultraviolet spectra of many aromatic compounds (38, 39, 40). It is evident that the absorption characteristics of protonated benzamide are equally compatible with an N- or an O-protonated structure, and are not exclusively in favor of the latter, as Hantzsch (4) assumed.

ACKNOWLEDGMENT

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A RADIOCHEMICAL TECHNIQUE FOR STUDYING RANGE-ENERGY RELATIONSHIPS FOR HEAVY IONS OF KEV ENERGIES IN ALUMINUM¹

J. A. DAVIES, J. FRIESEN,² AND J. D. MCINTYRE³

ABSTRACT

A rapid technique has been developed for dissolving successive thin layers of metal from the surface of an aluminum foil: viz. electrochemical oxidation at constant voltage in aqueous ammonium citrate, followed by removal of the oxide film in a phosphoric acid-chromic oxide solution. Due to the highly protective nature of the aluminum oxide film, this two-step process enables very uniform surface layers of metal as thin as $1 \mu\text{g}/\text{cm}^2$ to be removed. The total weight of aluminum dissolved increases with the applied anodic voltage at a rate of $0.30 \mu\text{g cm}^{-2} \text{ volt}^{-1}$ (approximately 11 Å per volt) over the range 0–150 volts. The technique should be sufficiently sensitive to study the depth of penetration in aluminum of radioactive ions with kinetic energies as low as a few kiloelectron volts.

An approximate value for the range of Na^{24} recoil atoms from the $\text{Al}^{27}(\alpha, \alpha')$ reaction was obtained. A more extensive application to range studies is given in the next paper.

INTRODUCTION

A great deal of attention has been devoted in recent years to studying the interaction of charged particles with matter. However, in the energy region below 1 Mev very few experimental data have been obtained on the range of heavy ions. A knowledge of the depth of penetration of ions of kev energies injected into solid materials is of interest from several points of view. It is of value in interpreting radiation damage and sputtering phenomena, and in preparing targets for nuclear research. From a theoretical viewpoint, such an investigation is of primary interest in the determination of the screened-interaction potential and of the mechanism of energy transfer in the elastic nuclear scattering of charged particles.

The current lack of experimental data may be attributed largely to the difficulties encountered in trying to measure extremely small depths of penetration. The mean range of a 45-kev Cs^{137} ion in aluminum, according to the Bohr-Nielsen theory (1), is about $5 \mu\text{g}/\text{cm}^2$, or 180 Å. Obviously, for ions of such short range, it would be difficult, if not impossible, to prepare sufficiently thin foils for studying the depth of penetration by conventional stacked-foil techniques.

The present work was undertaken in order to develop a sufficiently sensitive and reliable technique for carrying out range studies with heavy ions in the energy region 1–100 kev. The application of this technique in determining the range of alkali-metal ions as a function of energy will be presented in subsequent papers.

One approach to the problem has been reported recently by Baulch and Duncan (2). They used a gaseous absorber to study the range of radioactive recoil atoms from certain α -decay processes, and observed the effect of pressure on the number of recoil atoms reaching a collector plate. Unfortunately, the method is restricted to those few α -emitting nuclides that have a suitable radioactive daughter. Furthermore, since the energy of the recoil atom cannot be varied, the method is not capable of extensive application.

The approach in this laboratory has been to use a solid absorber, bombard it with a monoenergetic beam of radioactive ions, and then study the depth of penetration of

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²Present address: Department of Chemistry, University of Manitoba, Winnipeg, Manitoba.

³Present address: Department of Chemistry, Rensselaer Polytechnic Institute, Troy, N.Y., U.S.A.

ions into the target by removing successive uniform layers of target material and determining the amount of radioactivity in each. It was evident that mechanical methods would be far too coarse to remove sufficiently thin layers. Direct chemical or electrochemical etching of the surface is sensitive enough, but would almost certainly be non-uniform; corrosion phenomena are known to occur at very different rates at grain boundaries and impurity centers. Bredov and Okuneva (3) used chemical etching in an attempt to study the range of 4-kev Cs^{134} ions in germanium. They found that approximately 25% of the ions were not dissolved even after prolonged etching, and concluded that some of the ions must have penetrated several thousand angstroms into the target. However, this abnormal result could equally well be attributed to non-uniform etching of the surface.

We therefore selected a two-stage process, electrochemical formation of a uniform protective film, followed by chemical removal of the film, as the most promising possibility for further study.

It is well known that certain metals such as aluminum produce a thin highly protective oxide film when subjected to anodic oxidation in a suitable buffered electrolyte. If the oxidation is carried out at constant voltage, then within a few minutes the film thickness approaches an almost constant value. This value increases almost linearly with the applied voltage up to several hundred volts. Furthermore, according to Charlesby (4) the anodic current forming the film depends so markedly on the voltage gradient that the resulting film should be extremely uniform in thickness. Finally, Lewis and Plumb (5) have shown that a hot aqueous solution of phosphoric acid and chromium trioxide will rapidly dissolve the aluminum oxide layer without appreciably attacking the underlying aluminum metal. By using P^{32} and Cr^{51} , they demonstrated that such a treatment replaced the anodic layer with a highly protective mixed oxide film approximately 10 Å thick.

Provided the mixed oxide does not interfere with subsequent anodic oxidation, it should be possible to remove successive uniform layers of aluminum by this two-step process. However, the relationship between film thickness and applied voltage had not been determined previously below 15 volts (approximately 200 Å). It was therefore necessary to investigate film thicknesses at lower voltages in order to obtain sufficient sensitivity for the proposed range studies.

EXPERIMENTAL

Materials

The aluminum targets used throughout this work were prepared from superpure aluminum foil, 0.020-in. thick, by careful manual polishing with successively finer grades of metallurgical paper and then electropolishing for 60 minutes in a perchloric acid - acetic anhydride bath, according to the method outlined by Tegart (6). The resulting surface had a mirror-like finish; and hence surface irregularities must be considerably less than the wavelength of visible light. Immediately before use, each foil was anodized at 100 volts and then dipped in hot phosphoric acid - chromium trioxide solution to remove the resulting thick layer of aluminum oxide. This preanodizing treatment reduced the effective surface area of the foil by approximately 30% (see Fig. 2), presumably by removing submicroscopic irregularities, and gave a reproducibly flat surface.

Anodizing Step

The anodizing bath consisted of an aqueous solution of C.P. ammonium citrate (30 g per liter), maintained at $25 \pm 0.5^\circ \text{C}$ in a 200-ml aluminum beaker which served as cathode.

The aluminum sample to be anodized was suspended in the center of the beaker by an aluminum wire, and the desired voltage provided from a bank of storage batteries. In some of the early runs, a calomel reference electrode was occasionally inserted into the bath to measure the voltage across the anodic film. However, except at the start of a run, this voltage was very close to the total applied voltage across the cell; since chloride ion is small enough to penetrate the aluminum oxide film and thereby interfere with the electrolytic process, the use of a reference electrode was discontinued in subsequent runs, and the anodic voltage was assumed to be identical with the total applied voltage.

Film-Stripping Step

Rapid dissolution of these aluminum oxide layers was accomplished by immersing the anodized aluminum samples in a hot aqueous solution of orthophosphoric acid (50 g per liter) and chromium trioxide (30 g per liter). Provided the temperature of the solution was maintained above 90° C, a 2-minute treatment completely removed even a 100-volt film.

Aluminum Analysis

The thickness of the oxide layers was determined by neutron activation analysis. Three samples of known area were cut from each anodized foil, and inserted in a nylon capsule along with an aluminum standard (approximately 100 μ g Al wire). The capsule was then irradiated for 30 seconds in the pneumatic carrier (7) of NRX at a flux of 6.8×10^{13} neutrons per square centimeter per second. After irradiation the anodized aluminum was placed in the stripping solution in order to dissolve the oxide layer, and the amount of Al^{28} activity in solution determined with a well-type NaI scintillation counter. By comparing this activity with that obtained from the aluminum standard, which had been dissolved in sodium hydroxide solution to provide comparable geometry and absorption, the amount of aluminum in the oxide layer can be readily calculated. Due to the high neutron flux and rapid delivery time available, the method was sufficiently sensitive to determine 0.1 μ g of aluminum. In view of the short half-life of Al^{28} (2.3 minutes), this was considered quite satisfactory.

With the exception of the films formed at zero applied voltage, a standard deviation of less than 5% was obtained. At zero voltage, the deviation was much larger (approximately 20%). This is probably due to the presence of a thin highly protective film produced on the aluminum surface by CrO_3 (5) during the preanodizing treatment. In the absence of an applied potential, this film probably continues to exert sufficient protection, even after removal from the stripping solution, to inhibit partially the subsequent oxidation process.

RESULTS AND DISCUSSION

In order to determine how rapidly the phosphoric acid - chromic oxide stripping solution dissolved an aluminum oxide barrier layer, two pieces of aluminum were anodized at 25 volts, irradiated in NRX, and then immediately immersed in stripping solution, one at 50° C, and the other at 90° C. Aliquots were removed at various times, and counted to determine the amount of aluminum that had dissolved (Table I).

A standard 2-minute treatment is evidently sufficient to remove the oxide layer completely, provided the temperature is maintained at 90° C. At the lower temperature, however, stripping was far from complete, even after 10 minutes.

In order to investigate the relationship between oxide film thickness and anodic voltage, a series of foils were anodized at different voltages from 0 to 30 volts. In each case the electrolysis was carried out at constant voltage for approximately 10 minutes.

TABLE I
Efficiency of film stripping by $\text{H}_3\text{PO}_4\text{-CrO}_3$ solution

Time in $\text{H}_3\text{PO}_4\text{-CrO}_3$ solution (minutes)	c.p.m. of Al^{28} (normalized for decay)	
	At 50° C	At 90° C
0.5	—	42,300
1.0	3,140	42,000
2.0	5,600	43,200
5.0	18,100	44,000
10.0	35,500	43,300

A typical curve of current vs. time is shown in Fig. 1, with a change of abscissa after the first 60 seconds. It is evident that the rate of film formation, which is directly related to the anodic current, falls very rapidly in the first few seconds, but gradually approaches an almost constant value. Walkenhorst (8) showed that, after 1 hour, the rate of film

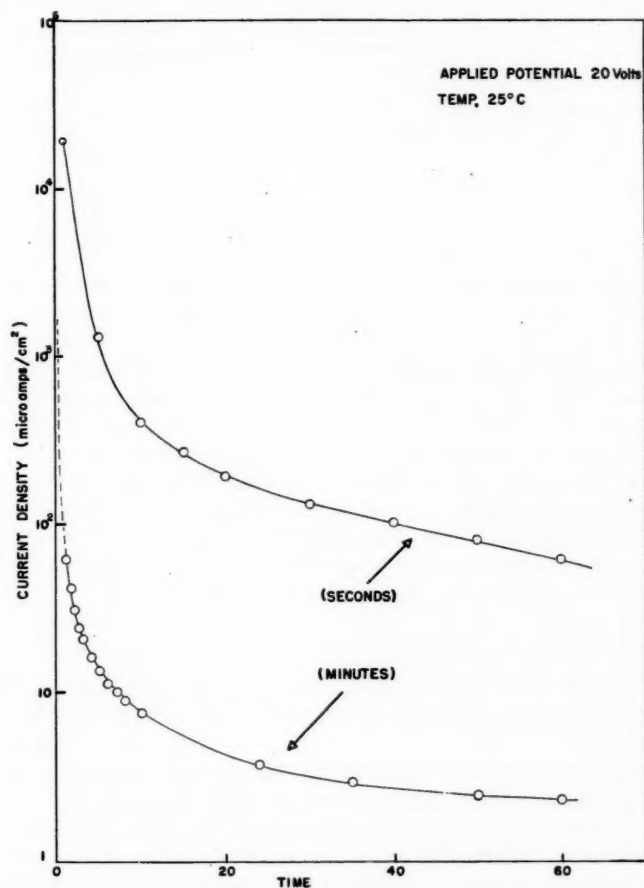


FIG. 1. Anodization of aluminum: current-time relationship.

growth had decreased to less than 1% per hour. A somewhat shorter time of 10 minutes was selected as the standard anodic treatment in the present investigation, so as to permit future range studies to be carried out with fairly short-lived isotopes. Even after 10 minutes, the film formation current had usually fallen below 7 microamperes/cm², which is equivalent to a rate of aluminum oxidation of less than 1 Å per minute.

The effect of voltage on film thickness is illustrated in Fig. 2. Some of the foils had not

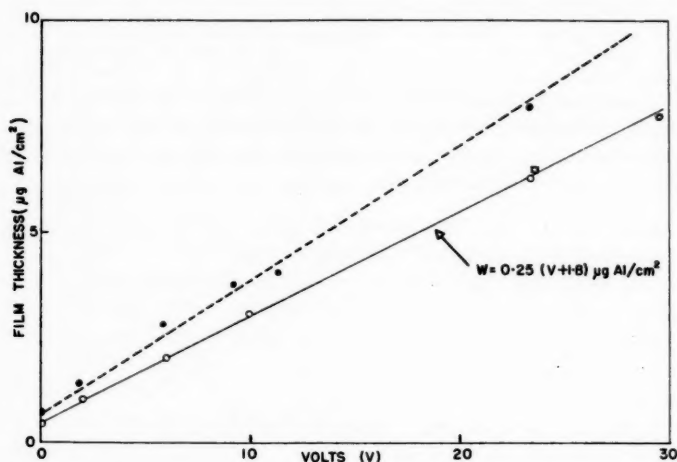


FIG. 2. Graph of film thickness ($\mu\text{g Al cm}^{-2}$) vs. the applied voltage (V). Number of preanodizing treatments: ● none, ○ one, □ four.

been subjected to any preanodizing treatment. In both cases, a linear relationship was observed. However, with preanodized foils, the slope was considerably less. This can probably be interpreted as a reduction in the true surface area caused by the removal of a thick uniform oxide layer in the preanodizing treatment. No further reduction in surface area occurred even after three additional preanodizing steps. It was concluded, therefore, that one such treatment was sufficient to produce a very reproducible surface. All further work was carried out only with preanodized foils.

The relationship between film thickness (W) in micrograms of aluminum per square centimeter and the applied voltage (V) may be expressed as follows:

$$[1] \quad W = 0.25 \times (V + 1.8).$$

The "effective" voltage (1.8 volts) required to account for the observed thickness at zero applied voltage agreed quite closely with the standard electrochemical potential of aluminum of 1.66 volts.

If the oxide consists largely of unhydrated Al_2O_3 , as X-ray studies on thicker films suggest (9), then the above value of $0.25 \mu\text{g cm}^{-2} \text{ volt}^{-1}$ for the weight of aluminum in the oxide film is equivalent to a total oxide film thickness of $0.475 \mu\text{g cm}^{-2} \text{ volt}^{-1}$. This is in good agreement with previously published values of 0.47 to $0.50 \mu\text{g cm}^{-2} \text{ volt}^{-1}$ (8, 10, 11) which were observed at much higher voltages (30–580 volts) by determining the decrease in weight on stripping off the oxide.

In order to study the depth of penetration of radioactive ions in aluminum, it is necessary to know the total amount of aluminum removed in the anodizing plus stripping operation. In the above experiments, we have investigated only the amount that is removed during the stripping process, i.e. the thickness of the protective oxide film produced during the anodic oxidation. However, it has been suggested (12, 13) that the efficiency of the anodic current in forming Al_2O_3 may be considerably less than 100%, and that a significant amount of aluminum ion may escape into solution during the anodic process. This would cause the total thickness of aluminum removed to be somewhat greater than that expressed by equation 1.

Several runs were therefore carried out to investigate the existence and importance of this effect. Pieces of aluminum foil were irradiated briefly in NRX, and were then subjected to anodic oxidation and film stripping as before. The amount of Al^{28} activity in both the anodizing and the stripping solutions was measured, and the results are tabulated in Table II. Over the range studied (18–100 volts), the ratio of Al^{28} activities in the

TABLE II
Loss of Al^{+++} during anodizing

Applied voltage, volts	Al^{28} activity (c.p.m.) in:		Ratio, A/B
	Anodizing solution	Stripping solution	
	A	B	
18	2010	9900	0.20
18	1080	5080	0.21
18	1260	7400	0.17
100	8730	41,000	0.21

two solutions remained constant; hence it is evident that a correction of 20% must be applied to equation 1 to account for the loss of aluminum during the anodizing step. The total weight (W) of aluminum removed by anodic oxidation plus film stripping may be expressed as

$$[2] \quad W = 0.30 (V+1.8).$$

Due to the short half-life of Al^{28} , the counting rates after 10-minute anodizing treatment had become very small and this investigation could not be extended to lower voltages. However, it would seem reasonable to assume that the fraction of aluminum ions lost in the anodizing step would remain almost constant over the total voltage range of interest to us.

It may be concluded, from the above studies, that layers of aluminum as thin as $1 \mu\text{g cm}^{-2}$ may be removed rapidly and reproducibly. This would permit range-distribution studies in aluminum to be carried out with radioactive ions having kinetic energies as low as a few kiloelectron volts (see following paper).

Na^{24} Recoil Atoms

An additional check on the reproducibility of the anodizing and film-stripping techniques for removing layers of aluminum of known thickness was obtained by studying the distribution of the Na^{24} atoms produced by the (n,α) nuclear reaction on aluminum. Samples of aluminum, wrapped in cadmium to prevent thermal neutron side-reactions, were irradiated for 15 hours in the NRX reactor, and allowed to decay for at least 12 hours to eliminate the short-lived Mg^{27} and Al^{28} activities. The Na^{24} distribution as a

function of depth was then determined by removing successive layers of aluminum of various thicknesses and counting the resulting solutions. A well-type NaI crystal was used as previously, but with a pulse-height selector set to record only those γ -pulses that exceeded 2.0 Mev. Under these conditions, the total contribution from the most significant impurities in superpure aluminum (14), viz. Cu, Ga, Sc, Mn, La, and Co, amounted to less than 0.05% of the Na^{24} activity. It should be noted that, due to the small cross section for the (n, α) reaction, low counting rates of Na^{24} were involved: for example, with a 20-volt film, the Na^{24} activity was approximately 100 c.p.m., which is only three times the background counting rate. Consequently, statistical counting errors were rather large, in some cases, as high as 15%. Thicker oxide films (up to 150 volts) were used in order to reduce this error.

The $\text{Al}^{27}(n, \alpha)\text{Na}^{24}$ reaction is endothermic by approximately 3.3 Mev, and can only occur with high-energy neutrons. Since fast neutrons are not significantly attenuated in passing through a thin foil of aluminum, it is evident that the rate of production of Na^{24} atoms will be uniform throughout the foil. However, those formed within their recoil range of the surface will have a finite probability of escaping. The Na^{24} distribution, therefore, should increase at first with increasing depth below the original surface, and gradually approach a constant value. A graph of the actual distribution observed in a typical run is shown in Fig. 3. The thickness of each layer was calculated from the anodic voltage by means of equation 2. After about 5000 Å of aluminum was removed, the Na^{24} content did approach a constant value. In Table III, this constant value is compared with the average Na^{24} content for the whole foil. The latter quantity was determined by

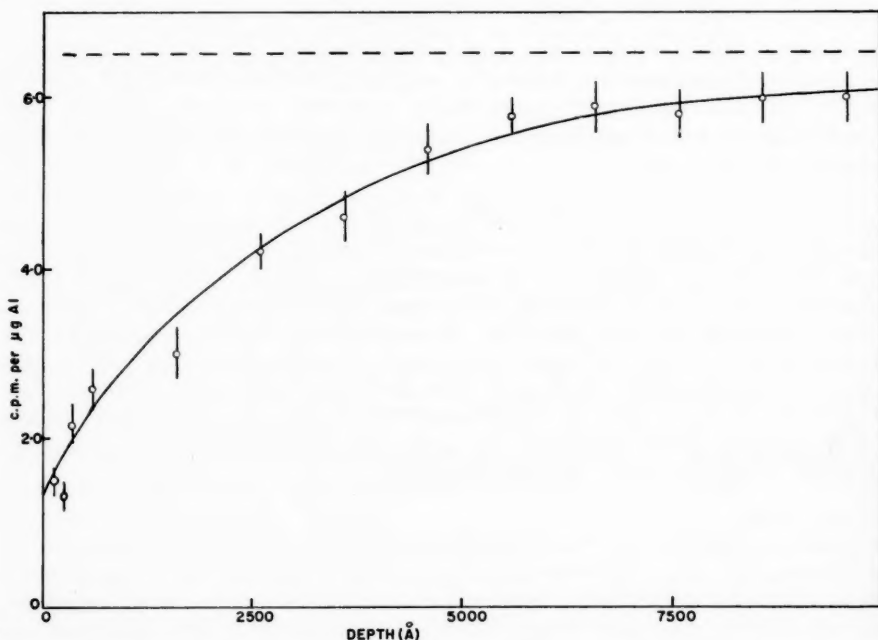


FIG. 3. Distribution of Na^{24} recoil atoms vs. depth below surface of foil. Dotted line represents average Na^{24} content of the whole foil.

TABLE III
Comparison of Na^{24} content in a thin layer with Na^{24} content for the whole foil

Run No.	Na^{24} content (c.p.m./ μg Al) of:		Ratio, A/B
	Thin layer	Total foil	
	A	B	
2	5.49	5.78	0.95 ₀
3	4.34	4.62	0.94 ₀
4	4.55	4.89	0.93 ₀
5	5.50	5.40	1.0 ₂

completely dissolving a piece of the foil of known weight, and measuring the Na^{24} activity in a small aliquot. The agreement between the two confirms the validity of equation 2 up to at least 150 volts.

In one run, 25 successive layers were removed at an applied potential of 100 volts in order to test the reproducibility of the technique. In every fifth layer, the Na^{24} content was measured by counting both the anodizing and stripping solutions. Also, the foil was weighed in order to determine directly the average weight loss for the previous five layers. The results are summarized in Table IV. Both the weight loss and the Na^{24} content

TABLE IV
Reproducibility of anodizing process

Number of 100-v layers removed	Average weight loss/100 v for previous five layers ($\mu\text{g}/\text{cm}^2$)	Na^{24} content in last layer (c.p.m./ cm^2)
5	28.5	121
10	28.0	136
15	29.5	130
20	29.0	140
25	28.5	139
Calculated value per 100-v layer (from equation 2)	30.5	138

remained almost constant throughout, thereby indicating that the process may be repeated a large number of times without significantly affecting the voltage-thickness relationship. The somewhat lower value obtained in layer 5 for the Na^{24} content may be attributed to recoil loss which, according to Fig. 3, should be quite significant for the first six to eight layers. Good agreement was obtained between the observed values and those calculated from equation 2 both for the weight loss, and for the Na^{24} content per 100-volt layer. This provides an excellent cross-check on the validity of equation 2.

One might think that the variation of Na^{24} activity with depth, illustrated in Fig. 3, might be used to provide quantitative information about the range of the Na^{24} recoil atoms themselves; but, unfortunately, this was not possible. First of all, the recoil atoms were not collimated and therefore a geometric factor would have to be introduced to correlate the number of atoms escaping from a given depth below the surface with the range. This factor, in turn, would depend to some extent on the shape of the recoil track which, due to elastic scattering, would certainly not be linear.

Furthermore, the recoil atoms were not monoenergetic; their energy depended markedly on the energy of the incident neutron and on the angular correlation between it and the emitted α -particle. Using the most recent data for the (n, α) cross section (15) and for the neutron spectrum in NRX, it was estimated that 90% of the recoils would occur between 0.1 and 2.0 Mev, provided there is little or no correlation in the center of mass system between the direction of the incident neutron and the emitted α -particle. A strong angular correlation, although considered very unlikely in an (n, α) reaction, would shift the energy limits for the recoil atoms to much lower values (0.04 and 0.3 Mev, respectively).

It is evident from Fig. 3 that only a very small number of Na^{24} atoms, originating at a depth greater than 10,000 Å below the surface, manage to escape. This implies that the mean range of a 2-Mev Na^{24} atom in aluminum is somewhat less than 10,000 Å.

SUMMARY

Successive uniform layers of known thickness can be removed from an Al target by a two-stage process, consisting of anodic oxidation followed by chemical dissolving of the film. The thickness removed varies linearly with the applied voltage. Reproducible results were obtained with layers as thin as 1.0 μg per cm^2 (37 Å) of aluminum, which suggests that the method should be sufficiently sensitive for studying the range of radioactive ions with kinetic energies as low as a few kiloelectron volts.

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THE RANGE OF ALKALI METAL IONS OF KILOELECTRON VOLT ENERGIES IN ALUMINUM¹

J. A. DAVIES, J. D. MCINTYRE,² R. L. CUSHING, AND M. LOUNSBURY

ABSTRACT

A simple electrostatic accelerator capable of producing a monoenergetic beam of alkali metal ions at energies up to 100 kev has been used to study the range of Cs¹³⁷ ions in aluminum as a function of energy. The median range (R_M) increases linearly with energy as predicted from the Bohr-Nielsen equation, but has a value about twice that predicted by this equation. Furthermore, the observed straggling about the mean value is not Gaussian in shape, but consists of an asymmetric peak with a pronounced exponential "tail". The possible significance of these results is discussed. Preliminary results are given for the range of 30-kev Rb⁸⁶ and Na²⁴ ions in aluminum.

INTRODUCTION

The present study has been undertaken as part of a program to obtain precise experimental measurements on the penetration depth and distribution of heavy atomic particles in matter at bombardment energies up to 100 kev. As pointed out by Nielsen (1) this is a velocity region of very considerable importance, both from the theoretical and practical viewpoint. The ion is moving sufficiently slowly for elastic nuclear collision to predominate over ionization as the principal mode of energy loss; hence range studies are of considerable interest for comparison with theoretical predictions of the cross section and mechanics of energy transfer in the elastic scattering process. Furthermore, since nuclear collision is far more effective than ionization in producing atomic displacements, this is also the region in which maximum radiation damage and sputtering should occur.

However, because of the experimental difficulties associated with measuring small depths of penetration, there have been until now almost no reliable experimental results reported on the range of heavy particles below 100 kev.

Our experimental technique consists in bombarding an aluminum target with a monoenergetic beam of radioactive ions of desired energy, and then determining the distribution of radioactivity as a function of depth by dissolving successive very thin uniform layers of aluminum of known thickness—using the electrochemical method described in the previous paper (2).

EXPERIMENTAL

The accelerator used for producing the beam of radioactive ions was designed and constructed specially for these range studies. Considerable economy and flexibility in design were achieved by carrying out the acceleration in two separate stages (see Fig. 1). In the first or low-energy stage, a beam of positive ions is produced in a thermionic-emission ion source A of the single-filament type (3). It consists of a tantalum ribbon upon which is evaporated a solution containing approximately 10^{-7} g of (Cs¹³⁷)₂SO₄, and produces a beam of Cs¹³⁷ ions at currents up to 10^{-6} amp. The filament is maintained at a positive potential of up to 5 kv in order to provide the first stage of acceleration. In the second stage, the beam passes between a set of four monitoring plates F, each of which is connected to an electrometer, and is then accelerated towards the target G,

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²Present address: Department of Chemistry, Rensselaer Polytechnic Institute, Troy, N.Y., U.S.A.

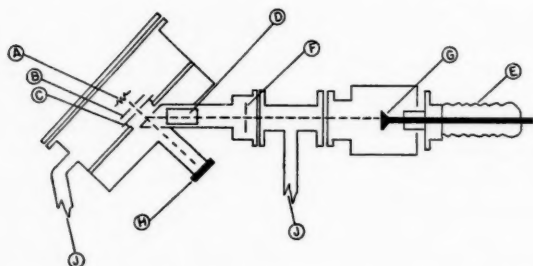


FIG. 1. Schematic diagram of ion accelerator: (A) ion filament, (B) grounded defining slit, (C), (D) beam-alignment plates, (E) high-voltage polystyrene insulator, (F) monitoring plates (4), (G) target, (H) Faraday cup, (J) to diffusion pumps.

which is maintained at any required negative potential up to 120 kv. In this way, the problem of maintaining an ion source at high voltage is eliminated. For energies up to 5 kev, the required voltage can be provided by the first stage alone, and in such cases the second stage is connected directly to ground.

Between the two stages, the beam passes between two pairs of plates C and D; an adjustable voltage is applied across each pair in order to align the beam on the target. One set of plates C deflects the beam through an angle of 30° in order to separate the ions completely from any neutral, and hence unaccelerated, atoms. The ion current is determined intermittently by reducing the deflecting voltage across C to zero, thereby permitting the ions to enter the Faraday cup H. The ion current is determined on a Keithley Electrometer Model 200 capable of measuring currents down to 10^{-13} amp with an accuracy of $\pm 2\%$.

In order to minimize radiation damage and contamination effects, it is desirable to bombard as large an area of the target as possible. Hence, there is no need to provide any focusing. Indeed, the cross-sectional area of the beam is considerably smaller than the normal target area (4 cm^2), and therefore, in most runs, the beam is traversed back and forth across the target to increase the bombarded area. This is accomplished by gradually varying the voltages on C and D during the bombardment until current begins to register on one or other of the monitoring plates at F. These four plates are positioned at 90° with respect to one another, and can be adjusted to define accurately the desired area of target to be bombarded. In Fig. 2, a curve of ion current falling on

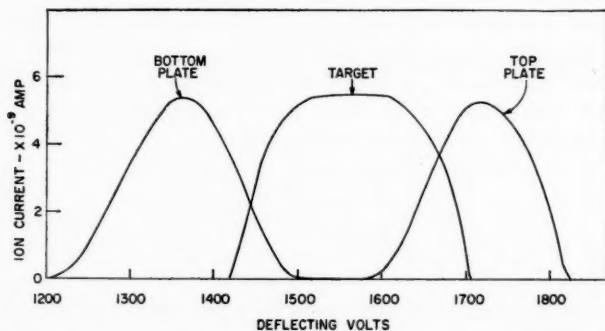


FIG. 2. Ion current on monitoring plates and target as a function of deflecting voltage. Accelerating voltage 3 kv.

two of these monitoring plates and on the target is shown as a function of the deflecting voltage across C.

A differential pumping system is used, consisting of two high-speed oil-diffusion pumps, one connected to the source chamber, and the other to the target chamber. The normal operating pressure along the path of the beam is about 2×10^{-6} mm. The total path length is 30 cm.

The adjustable accelerating voltage for the second stage is provided by a New Jersey Electronics 120-kv power supply Model HL-80 stabilized to $\pm 2\%$.

PROCEDURE

Aluminum targets, approximately 2.5×2.5 cm, were cut from strips of 0.020-in. "super-pure" aluminum foil which had been carefully electropolished and preanodized to provide a reproducibly flat surface. The final stage of this treatment, removal of a thick anodic oxide film, was carried out immediately before the target was loaded into the accelerator in order to minimize the thickness of the surface oxide layer formed by action of air on the aluminum. After the bombardment was completed, the radioactivity of the target was measured to determine the number of Cs^{137} ions embedded in it, and then a series of uniform layers were removed by successive anodic oxidation and film stripping, as described in the preceding paper (2).

By varying the applied voltage in the oxidation step, layers of aluminum of any desired thickness from 37 Å to 1000 Å could be prepared for stripping. After one anodic oxide film had been stripped off, the target was rinsed with ethyl alcohol, allowed to dry, and counted. The process was then repeated until all the Cs^{137} ions had been removed from the target. The activity of the target was measured with an end-window flow-type proportional counter having a geometrical efficiency of approximately 30%.

The amount of Cs^{137} contained in each layer was determined from the decrease in the amount of residual radioactivity in the target. In some runs, to perform a mass balance, the Cs^{137} content in each layer was also determined directly by measuring the radioactivity in aliquots from the anodizing and film-stripping solutions. Good agreement was obtained between the two methods; however, in practice, the latter was much more tedious. Very small aliquots had to be used to avoid errors due to source thickness, and consequently the counting rates involved were very low. Therefore, in most of the runs, the Cs^{137} content per layer was determined solely from the decrease in target activity.

It should perhaps be noted that the depth of penetration of Cs^{137} ions into the target is sufficiently small to neglect any subsequent attenuation of the emitted β -particles. This was verified by placing a thin aluminum absorber (2 mg/cm^2) over the target. The counting rate decreased by 2.1%. Even at 50 keV, the average depth of penetration of Cs^{137} in aluminum was only 0.01 mg/cm^2 , and hence the attenuation of β -particles was negligible.

RESULTS

A typical run illustrating the determination of the Cs^{137} distribution in a bombarded target is shown in Table I. The two different methods (columns 6 and 7) for obtaining the Cs^{137} activity in each layer are in satisfactory agreement. The thickness (W) per layer (column 3) has been calculated directly from the anodic voltage V by using the relationship from the preceding paper (2): viz. $W = 0.30 (V + 1.8)$. It will be noted that the first layer contains an extra $0.5 \text{ } \mu\text{g/cm}^2$. This represents a small correction term which is applied to all runs in order to take account of the oxygen that is present

TABLE I
Distribution of 50-kev Cs¹³⁷ ions in aluminum target

(1) Layer number	(2) Anodic voltage	(3) Amount of Al (W) in oxide layer (μg/cm ²)	(4) Total amount removed (μg/cm ²)	(5) Residual target activity (c.p.m.)	(6) Cs ¹³⁷ activity (c.p.m.) per layer:		(7)
					Calculated from col. 5	By direct measurement	
0				59,920			
1	5.5	2.2+0.5	2.7	59,550	370	520	
2	3.9	1.7	4.4	58,760	790	880	
3	3.9	1.7	6.1	55,255	3505	3940	
4	3.9	1.7	7.8	46,885	8370	8080	
5	3.9	1.7	9.5	36,920	9965	9670	
6	3.9	1.7	11.2	28,330	8590	8710	
7	3.9	1.7	12.9	21,380	6950	6580	
8	3.9	1.7	14.6	16,840	4540	4610	
9	3.9	1.7	16.3	13,635	3205	3240	
10	11.8	4.1	20.4	8,100	5535	5470	
11	11.8	4.1	24.5	4,970	3130	3080	
12	11.8	4.1	28.6	3,172	1798	1850	
13	11.8	4.1	32.7	2,097	1075	1195	
14	23.8	7.7	40.4	875	1222	1205	
15	23.8	7.7	48.1	456	419	—	
16	23.8	7.7	55.8	172	284	—	
17	23.8	7.7	63.5	78	94	—	
18	23.8	7.7	71.2	30	48	—	

during the bombardment as an oxide layer on the target surface, and which contributes therefore to the slowing down of the ion beam. The aluminum content of this oxide layer is included in the above expression for W . It is assumed that the aluminum and oxygen atoms have comparable stopping power for heavy ions. This assumption should be valid provided the ion range is considerably greater than $0.5 \mu\text{g}/\text{cm}^2$.

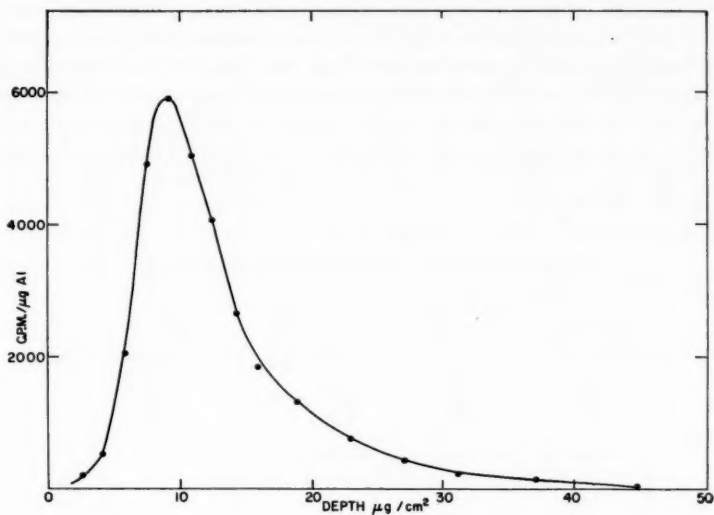
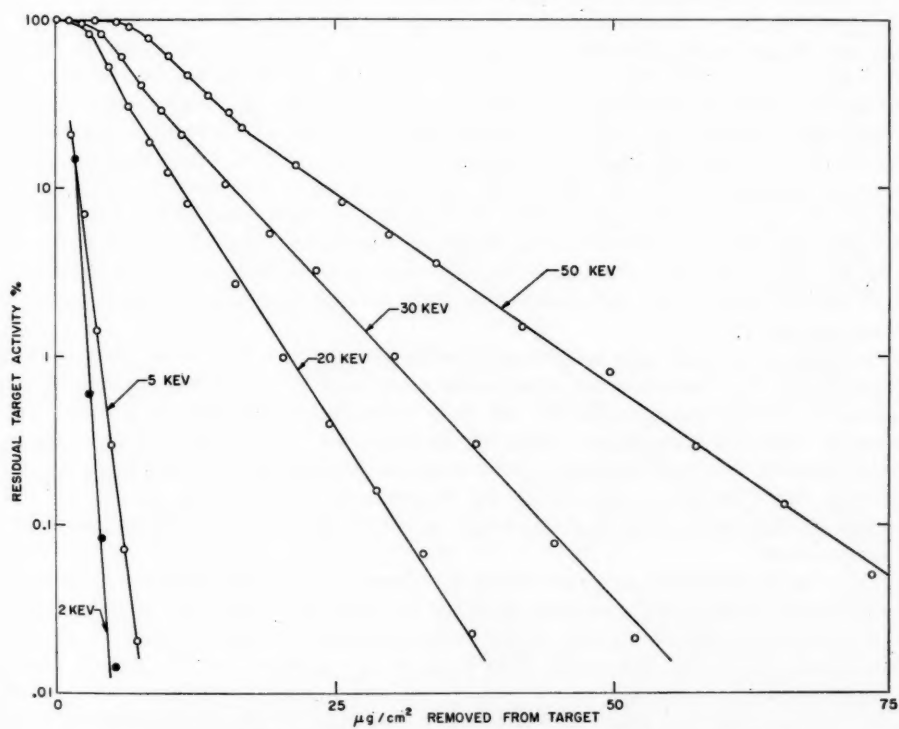
The actual distribution of Cs¹³⁷ ions in the target was observed to be markedly asymmetric. This may be seen more clearly in Fig. 3, in which the Cs¹³⁷ content in each successive layer is plotted against the depth beneath the original surface. The existence of an appreciable, highly penetrating "tail" in the distribution curve is a characteristic feature of these range studies; as a result, the median range R_M , i.e. the thickness required to stop 50% of the incident ions, is somewhat greater than the most probable value R_P . Both R_M and R_P increase linearly with energy (Table II).

Typical distribution curves for Cs¹³⁷ ions of various energies are shown in Fig. 4, in

TABLE II
Range of Cs¹³⁷ ions in aluminum

Energy (kev)	R_P/E (μg cm ⁻² kev ⁻¹)	R_M/E (μg cm ⁻² kev ⁻¹)	$X_{1/2}/E$ (μg cm ⁻² kev ⁻¹)
2*	—	$0.3 \pm .1_5$	$0.20 \pm .05$
5*	—	$0.2 \pm .06$	$0.12 \pm .02$
20	$0.20 \pm .03$	$0.24 \pm .02$	$0.14_5 \pm .01$
30	$0.19 \pm .02$	$0.25 \pm .01$	$0.13 \pm .01$
50	$0.19 \pm .01$	$0.23 \pm .01$	$0.13 \pm .01$

*Depth of penetration too small to observe R_P , as the first layer contained more than 50% of Cs¹³⁷ ions. R_M was obtained from Fig. 4 by extrapolation.

FIG. 3. Depth of penetration of 50-keV Cs^{137} ions in aluminum.FIG. 4. Distribution curves for Cs^{137} ions of various energies in aluminum.

which the residual activity remaining in the target has been plotted against the total thickness of aluminum removed. In each case, apart from an initial region, the activity falls off exponentially with depth. The half-thickness, $X_{1/2}$, of this exponential region also was observed to increase linearly with the energy of the incident ion.

In order to test the reproducibility of the technique, several runs were carried out at 30 kev under various experimental conditions (see Table III).

TABLE III
Test of reproducibility: 30-kev Cs^{137} ions in aluminum

Run No.	Ion current (μamp)	Total number of Cs ions	R_p ($\mu\text{g}/\text{cm}^2$)
1	40	0.56×10^{13}	4.4
2	40	4.7	4.8
3	40	20*	4.8
4	600	3.8	4.5

* 4.0×10^{13} Cs^{137} ions, plus 16.0×10^{13} Cs^{133} ions.

In the first three runs, the duration of the ion bombardment was varied by a factor of 30 to investigate whether sputtering or radiation damage could alter significantly the initial distribution of the incident ions. The results indicate that prolonged bombardment does not change appreciably the observed value for the most probable range. In run 3, a further check on the absence of significant sputtering was provided by carrying out the bombardment in two stages: 4×10^{13} ions of Cs^{137} in the first stage, followed by a much larger number of inactive Cs^{133} ions in the second one. The observed distribution of Cs^{137} as a function of depth was identical with that in run 2, which showed clearly that the subsequent bombardment by inactive cesium had not changed the distribution of Cs^{137} . Furthermore, the radioactivity of the target was measured immediately before and after the second bombardment to determine whether any Cs^{137} had been sputtered from the target by the Cs^{133} ions. The observed decrease in activity was extremely small (0.3%), and in fact was not significantly greater than the statistical counting errors involved.

The absence of detectable sputtering or other secondary radiation damage in these range-distribution studies is not unexpected; even in run 3, the total number of ions striking the target was only 2×10^{14} and those were distributed over an area of 4 cm^2 . From the observed distribution curves for 30-kev ions in aluminum, it can readily be shown that the maximum ratio of cesium atoms to aluminum atoms in the target was less than 10^{-3} . Therefore, each cesium ion would have to eject an unreasonably large number of aluminum atoms from the target to reduce significantly the observed depth of penetration.

Run 4 was carried out at much higher ion current in order to investigate whether the observed distribution depended on the rate of energy deposition. It is true that in these experiments the rate of energy deposition was extremely small, usually less than 10 milliwatts; but, due to the short range of the incident ions, the kinetic energy is dissipated in an extremely small volume, equivalent to a power input of approximately one kilowatt per gram. It was thought that this high heat flux might give rise

to some secondary thermal effects. However, run 4 shows clearly that a 15-fold increase in the rate of energy deposition had no appreciable effect.

The distribution of Cs^{137} for each of the above runs is illustrated in Fig. 5. Within the statistical errors involved, the results for the four runs are indistinguishable.

Other Alkali Metal Ions

Some preliminary studies have also been carried out with 30-keV Na^{24} and Rb^{86} ions in aluminum. The results are illustrated in Fig. 6, and in Table IV. With both ions, a markedly asymmetric distribution curve is again observed. The energy dependence for these ions has not yet been investigated.

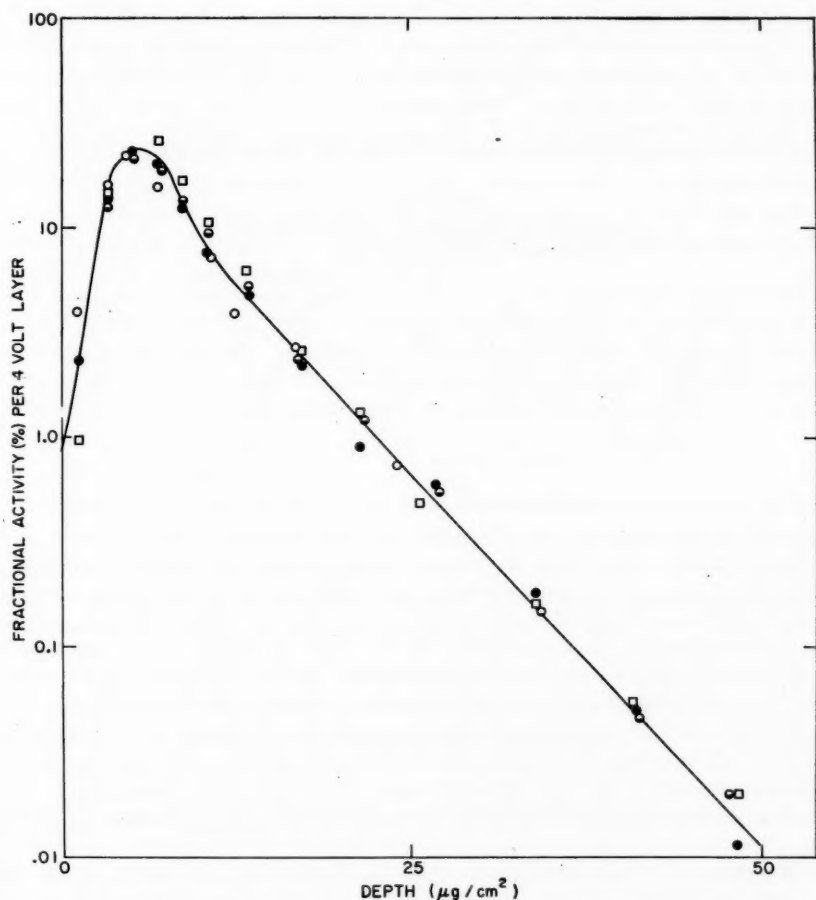
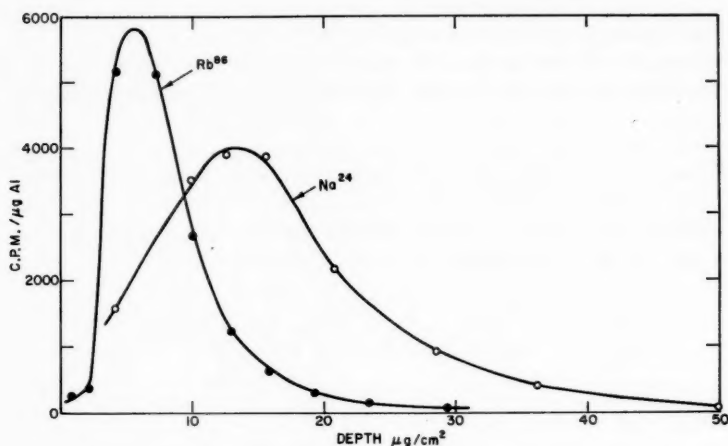


FIG. 5. Depth of penetration of 30-keV Cs^{137} ions in aluminum under different experimental conditions: ○ run 1, ◐ run 2, ● run 3, □ run 4.

FIG. 6. Depth of penetration of 30-keV Rb⁸⁶ and Na²⁴ ions in aluminum.TABLE IV
Range of 30-keV alkali-metal ions in aluminum

Ion	R_p ($\mu\text{g cm}^{-2}$)	R_M ($\mu\text{g cm}^{-2}$)	Range predicted by Bohr-Nielsen equation ($\mu\text{g cm}^{-2}$)
Na ²⁴	13.1	15.0	23.4
Rb ⁸⁶	6.6	8.4	5.4
Cs ¹³⁷	5.8	7.6	3.6
Na ²⁴ /Cs ¹³⁷	2.2	2.0	6.5

DISCUSSION OF RESULTS

Bohr (4) has shown that the complicated many-body problem involved in slowing down an atomic particle can be simplified considerably by separating it into two distinct types of collision processes: electronic or inelastic collisions, in which energy is transferred to individual electrons, thereby causing ionization or atomic excitation; and nuclear or elastic collisions, in which momentum and kinetic energy are transferred to the stopping atom as a whole. The former process is the more important at high velocity such as in the initial portion of a fission-fragment or alpha-particle track; whereas, when the moving particle has a velocity less than that of the slowest orbital electrons in the stopping material (viz. $<2 \times 10^8$ cm/sec), nuclear collisions tend to predominate. The ion velocities used in the present work were considerably less than this critical velocity; hence, nuclear collisions should be the more significant process throughout the range.

Nuclear collisions may be subdivided further into various types depending on the relative magnitude of the collision diameter, the screening parameter, and the wavelength of the incident particle. A general treatment of the problem is therefore quite complicated. However, at the energies studied in the present work, it has been shown by Nielsen (1) that, over the entire range, the collision diameter, or minimum distance of approach in a head-on collision in an unscreened coulomb field, is considerably larger

than the screening parameter. Hence, the nuclear collisions occur in a screened coulomb field. Furthermore, over most of the range, the wavelength of the incident ion is much smaller than the screening parameter and classical orbital considerations may be applied. For such a system the following range-energy relationship has been developed (1, 5):

$$\frac{R}{E} = 0.60 \frac{A_1 + A_2}{A_1} \cdot \frac{A_2}{Z_2} \cdot \frac{(Z_1^{2/3} + Z_2^{2/3})^{1/2}}{Z_1}$$

where R is the range in $\mu\text{g}/\text{cm}^2$, E is the energy of the incident particles in kev, A_1 , A_2 are the masses, and Z_1 , Z_2 are the atomic numbers of the incident and target atoms respectively.

The predicted linear relationship between range and energy is observed for Cs^{137} ions in aluminum (Table II). A comparison of the absolute magnitude of the experimental and predicted values for the range of 30-kev alkali-metal ions is given in Table IV. Clearly, the theoretical values do have the correct order of magnitude, but the predicted variation from Na^{24} to Cs^{137} is several times larger than that observed. This discrepancy may be ascribed partly to the fact that the theory gives the total distance travelled by the particle in coming to rest, not merely the depth of penetration beneath the target surface. One important characteristic (1) of screened-field scattering is that the angular distribution is almost isotropic in the center-of-mass system, in contrast with coulomb scattering where small angular deflections predominate. As a result, the individual ion tracks will be far from linear; hence the predicted ranges must be reduced somewhat before comparing with the experimental values.

In the case of Cs^{137} , this correction term is quite small. The mass of the incident particle is more than five times that of the target atom; hence, to conserve momentum, it can be shown that the maximum deflection per collision is only 12° . On the other hand, with Na^{24} , where the mass ratio is close to unity, individual deflections as large as 90° are possible, and consequently the depth of penetration will be much less than the total path length.

Effect of Surface Area

One problem of some concern in the interpretation of these range studies is the possible effect of surface non-uniformity on the measured depth of penetration. Consider a small segment of surface (Fig. 7) inclined at an angle θ to the plane of the target. Let the area of the segment be ΔA . If the target is bombarded uniformly by a collimated beam of ions, then the number striking ΔA is given by $N(\Delta A \cos \theta / A')$ where N is the total number of ions striking the target and A' is the apparent or measured area. Each of these ions, in traversing a thin uniform layer of thickness δ , travels a distance $\delta / \cos \theta$. Hence, the sum of the distances travelled by all the ions striking the segment is given by $N(\Delta A / A') \cdot \delta$, which is independent of θ . Integrating over the whole target, and dividing by N , we find that the average distance travelled per ion is $\delta \cdot (A / A')$, where A / A' is the ratio of the true to the apparent surface area of the target. It is obvious, therefore, that surface irregularities increase markedly the average path length travelled.

However, in calibrating the relationship between oxide film thickness and anodic voltage (2), it was not possible to measure the true film thickness δ , but only the apparent thickness δ' . It can readily be shown that $\delta' = \delta(A / A')$. Since the same type of surface was used in the preliminary calibration as in the subsequent depth of penetration studies, it can be seen that the average distance travelled per ion in traversing a uniform film is identical with the apparent film thickness. Consequently, the effects of non-uniformity cancel out in determining the average range.

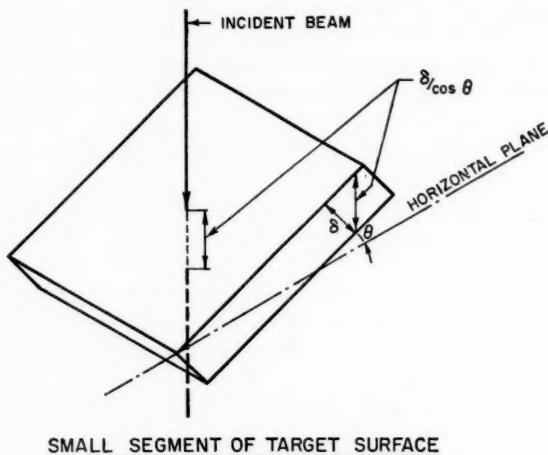


FIG. 7. Sketch to illustrate surface-area effect.

Of course, surface irregularities will introduce some straggling into the observed distribution, but this straggling should not be very marked: optically flat surfaces have been used throughout this work, and the preanodizing studies reported in the preceding paper (2) suggest that the ratio (A/A') is probably very close to unity.

A particularly interesting feature of our results is the observed asymmetric distribution. Some previous workers (6, 7) have assumed that the distribution of individual particle ranges about a mean value would be given approximately by an error curve:

$$W(R) = \frac{1}{\rho R_M \sqrt{2\pi}} \exp \left[-\frac{1}{2\rho^2} \left(\frac{R - R_M}{R_M} \right)^2 \right]$$

with a straggling parameter

$$\rho^2 = \frac{4}{3} \frac{A_1 A_2}{(A_1 + A_2)^2}$$

However, as noted by Bohr (4, p. 50), a Gaussian distribution occurs only when the maximum fractional energy transfer T_{\max} per collision is very small: in other words, when $A_1 \gg A_2$. This assumption is certainly not valid when using an aluminum target. Even with Cs^{137} , where $A_1 = 5.1 A_2$, T_{\max} is almost 0.60; and, assuming isotropic scattering, T_{av} is approximately 0.30. Since the range varies linearly with the energy, this means that each ion, on the average, traverses one-third of its total range before the first collision. Furthermore, since the collision diameter increases with decreasing energy of the incident ion, the mean free path should decrease markedly with every collision. Obviously, the depth of penetration is determined primarily by the first few collisions. Under such conditions, it can be shown (see Fig. 8, and Appendix) that the distribution curve consists of an asymmetric peak with a highly penetrating exponential "tail"; the half-thickness of the exponential region is determined by the mean free path for the first collision.

With Cs^{137} , this exponential "tail" is in fact observed. Furthermore, the half-thickness varies linearly with the energy, as would be expected.

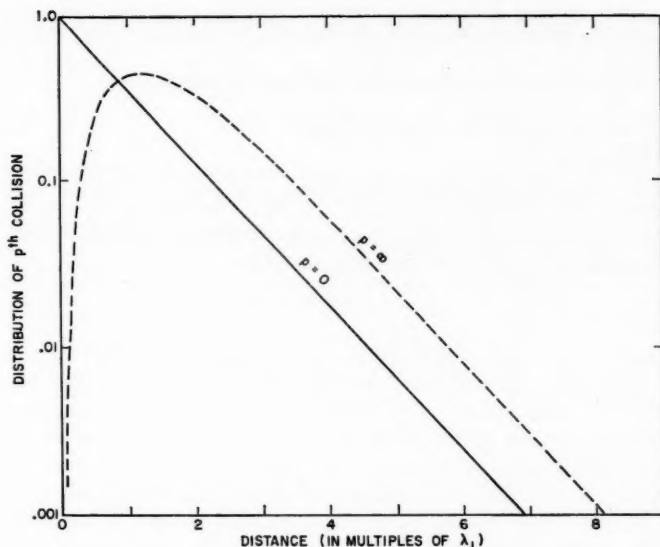


FIG. 8. Calculated distribution curves for large fractional energy loss per collision.

It is planned to extend these studies to somewhat higher energies, to other ions, and to other target materials in order to permit a more quantitative interpretation of the role of nuclear collisions in determining range-energy relations.

ACKNOWLEDGMENTS

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APPENDIX

CALCULATED RANGE DISTRIBUTION FOR LARGE ENERGY TRANSFERS

Consider an experiment in which N particles have been shot into the absorbing material. Suppose $N_p(r)$ is the number of particles that made p collisions in penetrating a distance r . Then the number that reached $(r+dr)$ making p collisions is the sum of

those that reached r making p collisions without making a further collision in dr and those that reached r in $(p-1)$ collisions and did make a collision in dr . That is

$$[1] \quad N_p(r+dr) = N_{p-1}(r)dr/\lambda_p + N_p(r)(1-dr/\lambda_{p+1})$$

where λ_p is the mean free path for the p th collision.

Writing $\mu = 1/\lambda$ gives

$$[2] \quad (d/dr)N_p(r) = \mu_p N_{p-1}(r) - \mu_{p+1} N_p(r).$$

This equation is the same, with r replacing time, as that governing a series of radioactive transformations, with the familiar solutions (8)

$$N_0(r) = N e^{-\mu_1 r}$$

$$N_1(r) = N \mu_1 \left(\frac{e^{-\mu_1 r}}{\mu_2 - \mu_1} + \frac{e^{-\mu_2 r}}{\mu_1 - \mu_2} \right)$$

etc.

and

$$[3] \quad N_p(r) = N \mu_1 \mu_2 \dots \mu_p \sum_{n=1}^{p+1} \frac{e^{-\mu_n r}}{a_n}$$

where

$$a_n = \prod_{i=1}^{p+1} (\mu_i - \mu_n), \quad i \neq n.$$

For the special case where the mean free path remains constant (i.e. where $\mu_1 = \mu_2 = \dots = \mu_p$), equation (3) becomes a Poisson distribution, which for large values of p is simply the familiar Gaussian curve. Such a condition would be approximately correct for a system in which the fractional energy loss per collision is small. However, where the energy transfer per collision is large, a very different type of distribution curve is obtained.

In order to illustrate this, let us take a somewhat idealized system in which the fractional energy transfer per collision is exactly 0.5. Clearly, in such a case, only the first few mean free paths contribute significantly to the total range. Since the mean free path is proportional to the energy, we may substitute in equation (3) the following relationship:

$$\mu_1 = \frac{1}{2} \mu_2 = \frac{1}{4} \mu_3 \dots = \frac{1}{2^{n-1}} \mu_n.$$

The resulting series

$$\sum_{n=1}^{\infty} \frac{1}{a_n} [\exp - (2^{n-1}) \mu_1 r]$$

is rapidly convergent and leads to the distribution shown in Fig. 8 by a dotted line: viz. an asymmetric peak, followed by an exponential region of half-thickness identical with that for the first collision.

The above treatment is greatly oversimplified and cannot be used for quantitative comparison with the observed distribution curves. No allowance has been made for variations in energy transfer from one collision to another, nor for the difference between the total path length and the depth of penetration.

ISOLATION AND STRUCTURE OF A NEW ALKALOID: ASPIDOCARPINE¹

STEWART McLEAN,² K. PALMER,² AND LÉO MARION

ABSTRACT

From the root bark of *Aspidosperma megalocarpon* Muell. Arg. a new alkaloid, aspidocarpine, has been isolated. It has the empirical formula $C_{22}H_{30}O_2N_2$ and contains an N-acetyl, one methoxyl group, and one active hydrogen. The alkaloid, a phenolic monoacidic tertiary base, has been shown by its properties, those of its derivatives, and the spectroscopic data, to contain an N-acetyl-6-methoxy-7-hydroxydihydroindole moiety. Oxidation of aspidocarpine with chromic acid gave rise to a product identical in all respects with apoaspidospermine obtained from the similar oxidation of aspidospermine. Since the structure of aspidospermine is known, the foregoing results establish the structure of the alkaloid aspidocarpine.

The root bark of *Aspidosperma megalocarpon* Muell. Arg., a tree that grows in British Guiana,³ has been found to contain alkaloids. They mostly occur in the petroleum ether extract, and largely consist (0.06% of dry weight) of one base which it is proposed to designate aspidocarpine. Its empirical formula derived from the analytical figures of the base and its salts is $C_{22}H_{30}O_2N_2$. Aspidocarpine melts at 168.5–169.5°, and determination of functional groups revealed that it contains one acetyl group, one methoxyl, one additional C-methyl besides that arising from the acetyl, and one active hydrogen.

The ultraviolet spectrum of aspidocarpine contains maxima at λ_{\max} 227 m μ , $\log \epsilon$ 4.42, and λ_{\max} 263.5 m μ , $\log \epsilon$ 3.92. It resembles that of aspidospermine and suggests that the new alkaloid, like aspidospermine, contains the N-acetyl-indoline chromophore. The spectrum of aspidocarpine was not affected by the presence of mineral acid, but was profoundly changed by the addition of sodium hydroxide.

In the infrared the spectrum of aspidocarpine contains no apparent hydroxyl absorption, but shows a peak at 1632 cm^{-1} which, although weak and at a low wave-number, must be indicative of the carboxyl of an N-acetyl group. Since, however, the base does not contain a carboxylic group, but contains an active hydrogen and is soluble in sodium hydroxide, since, further, it produces a pale olive-green color with ferric chloride, it must be phenolic. If the phenolic hydroxyl and the N-acetyl group were located sufficiently close to one another to form a strong hydrogen bond the effect in the infrared would shift the hydroxyl and carbonyl absorption to lower wave-numbers. Hence any hydroxyl absorption would be shifted to and covered by the CH stretching absorption region. The situation would thus parallel that observed in demethylaspidospermine (1). Evidence that this assumption is indeed correct has been obtained by blocking the hydroxyl function and thus removing the possibility of hydrogen bonding. Acetylation of the hydroxyl group was carried out smoothly in acetic anhydride and pyridine. The product, O-acetylaspidocarpine ($C_{24}H_{32}O_4N_2$) shows bands in the infrared at 1768 cm^{-1} and 1204 cm^{-1} characteristic of a phenolic O-acetyl (2) and another band at 1666 cm^{-1} due to the carbonyl of the N-acetyl group.

The phenolic hydroxyl of aspidocarpine did not react with diazomethane under the usual conditions, a common occurrence with strongly hydrogen-bonded phenols, but methylation was readily effected by the use of alkaline dimethylsulphate at room tempera-

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²National Research Council Postdoctorate Fellow.

³The plant material was obtained through the courtesy of Mr. R. Smeathers, Conservator of Forests, Kingston, Georgetown, British Guiana.

ture. The O-methylaspidocarpine ($C_{23}H_{32}O_4N_2$) thus produced showed a strong absorption band in the infrared at 1656 cm^{-1} due to the N-acetyl carbonyl. The ultraviolet spectra of both the O-acetyl and the O-methyl derivatives were not appreciably altered by sodium hydroxide. Thus when the phenolic hydroxyl is blocked and no hydrogen bonding is possible, the carbonyl absorption of the N-acetyl group in the infrared appears with its normal frequency and intensity.

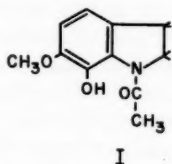
The N-acetyl group was characterized by hydrolysis of the alkaloid with sulphuric acid, steam-distillation of the reaction mixture, and spot-testing of the ethylamine salt of the distilled acetic acid on a paper chromatogram.

O-Methylaspidocarpine was hydrolyzed with 10% hydrochloric acid to O-methyl-deacetylaspido-*carpine* ($C_{21}H_{30}O_2N_2$). The infrared spectrum of this product no longer shows any carbonyl absorption, but contains a band at 3335 cm^{-1} attributable to an imino group. Treatment of the product with acetic anhydride and pyridine regenerates O-methylaspidocarpine, thus confirming the presence of an N-acetyl group in the alkaloid.

Treatment of aspidocarpine with hydrobromic acid produced an extremely unstable material which could not be crystallized. This material gives a blood red color with ferric chloride, which is consistent with an aminodihydric phenol. The material must be O-demethyl-N-deacetylaspido-*carpine* because on acetylation it is converted to O,O-diacetyl-O-demethylaspidocarpine ($C_{25}H_{32}O_6N_2$). The latter has an infrared absorption spectrum containing bands at 1777 and 1767 cm^{-1} ($C=O$) and 1204 cm^{-1} ($C-O$) due to two phenolic O-acetyl groups, as well as a band at 1668 cm^{-1} attributable to the non-bonded carbonyl of the N-acetyl group. This observation places the original methoxyl group of aspidocarpine in the aromatic ring. In support of this conclusion it has proved possible to hydrolyze selectively the O-acetyl groups of O,O-diacetyl-O-demethylaspidocarpine and isolate pure O-demethylaspidocarpine, $C_{21}H_{28}O_3N_2$, which has the characteristics of a dihydric phenol. In the infrared spectrum of this compound, as expected, the carbonyl absorption shows the effect of hydrogen bonding, and the hydroxyl region contains an absorption band attributable to the non-hydrogen-bonded hydroxyl group. Treatment of O-demethylaspidocarpine with diazomethane did not affect the original hydroxyl, which had already been shown to resist methylation by this method, but methylated the second hydroxyl, thus regenerating aspidocarpine.

O-Demethylaspidocarpine behaves as an ortho-dihydric phenol as shown by the following observations. With ferric chloride it produces initially an intense blue-green color, which on addition of sodium carbonate, changes to a very deep red, a color sequence characteristic of catechols. In a series of tests on the compounds already described it was observed that coupling with diazotized sulphanilic acid occurred whenever either the hydroxyl or the indoline nitrogen was free, but did not occur when both were substituted. This indicates that the positions in the benzene ring para to these two functions are unsubstituted. Attempts to oxidize aspidocarpine or O-demethylaspidocarpine with periodate by the method of Adler and Magnusson (3) failed to give any crystallizable products, but produced color sequences indicative of the formation of an ortho-quinone. The condensation of either the presumed crude quinone with ortho-phenylenediamine, or of O-demethylaspidocarpine with phosgene led invariably to amorphous products of doubtful composition. The product of the reaction with phosgene, however, showed in the infrared a peak at 1835 cm^{-1} , a value indicative of the formation of a cyclic carbonate. It is of some interest that O-methylaspidocarpine gives no color in the brucine test with

nitric acid and acetic acid, an observation in accordance with the model experiments of Lyons, Perkin, and Robinson (4), whereas aspidocarpine and O-demethylaspidocarpine both give a deep red color different from the characteristic brucinequinone color. The best evidence in favor of the ortho arrangement of the hydroxyl groups in O-demethylaspidocarpine came from an application of Jurd's method (5), which is based on the effect of buffered boric acid on the ultraviolet spectrum of a compound. The ultraviolet spectrum of O-demethylaspidocarpine shows a dramatic change in the presence of buffered boric acid and parallel experiments show that catechol undergoes a similar change while the other dihydroxybenzenes are unaffected. The spectrum of aspidocarpine is unaffected by buffered boric acid. The sum of the evidence therefore strongly favors partial structure I as representing rings A and B of aspidocarpine. The nuclear magnetic resonance evidence, discussed later, also supports this conclusion.



The close similarity between the chemistry of aspidocarpine and that of aspidospermine, as well as in the spectral properties of both alkaloids, is quite striking. The relationship in rings A and B has already been demonstrated. In the study of the saturated moiety of the molecule it has been found that the reactions of aspidocarpine parallel exactly those of aspidospermine including the rather remarkable rearrangements known to take place in the latter (6).

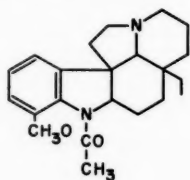
In line with aspidospermine (6, 7) aspidocarpine showed a high analytical N-methyl value (76% of calculated figure for one N-methyl) which later proved spurious, and still in keeping with other *Aspidosperma* alkaloids, O-methylaspidocarpine gave an N-methyl value considerably lower than that obtained with the alkaloid (24% of calculated value for one such group).

Aspidocarpine-N(b)-methiodide was readily prepared in dimethylformamide. It did not undergo the Hofmann degradation, however, but gave back aspidocarpine.

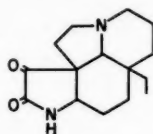
The von Braun degradation of aspidocarpine also produces a significant parallel with the behavior of aspidospermine in this reaction (6). Treatment of aspidocarpine with cyanogen bromide in chloroform (the reaction failed in benzene) gives rise to aspidocarpine bromocyanamide, $C_{22}H_{30}O_2N_3Br$, which exhibits the usual characteristics of this class of compounds, except that the normal solvolytic completion of the von Braun degradation fails since the bromocyanamide reverts to aspidocarpine even on reflux with ethanol.

These similarities between aspidospermine and aspidocarpine, coupled with their botanical relationship, suggested the possibility that they might differ only insofar as ring A was concerned. Ewins (8) had oxidized aspidospermine with chromic acid and had obtained a product, m.p. 193°, to which he tentatively assigned the structure of a keto-lactam (apoaspidospermine) resulting from the oxidative degradation of the

aromatic ring. The structure of aspidospermine (II) recently determined by X-ray crystallography⁴ (9) leads to structure III for apoaspidospermine,



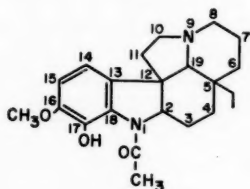
II



III

which should also be the product of the similar oxidation of aspidocarpine. Ewins' analytical figures were not in agreement with this structure but in our hands the oxidation of aspidospermine with chromic acid yielded a product, m.p. 224–225°, which gave analytical figures in excellent agreement with those required by III ($C_{18}H_{22}O_2N_2$). Both the infrared and ultraviolet spectra of the oxidation product were consonant with the presence of a five-membered keto-lactam in the molecule. This product was most probably identical with Ewins' apoaspidospermine, although it was purer as shown by the higher melting point. Aspidocarpine when oxidized with chromic acid yielded a product which had the same optical rotation and the same melting point as apoaspidospermine, alone or in admixture. The infrared spectra and the X-ray powder diagrams of both products were exactly superimposable.

The identity of the oxidation products of aspidocarpine and aspidospermine establishes the structure of the saturated moiety of the former, and this, together with the demonstration of the presence of a hydroxymethoxy-N-acetyl-indole in the molecule, affords conclusive proof that the structure of aspidocarpine is



IV

represented by formula IV. The assignment of the structure of the saturated part of the molecule depends on the X-ray crystallographic analysis of aspidospermine (9), and it follows from the identity of the oxidation products obtained from both alkaloids.

Aspidocarpine has proved very suitable for examination by nuclear magnetic resonance⁵ especially since the spectrum can be compared with that of aspidospermine, the structure of which has been conclusively established (9, 10).

⁴We acknowledge with thanks the courtesy of Professor N. S. Nyburg, who communicated to us the structure of aspidospermine in advance of his publication.

⁵Spectra were obtained with a Varian Associates high resolution nuclear magnetic resonance spectrometer operating at 60 Mc/s frequency. Chloroform was employed both as a solvent and as an internal reference; its proton resonance was assigned a value of zero c.p.s. and the scale was fixed from the position of the associated C^{13} (natural abundance) peaks which were shown to have a value of ± 105 c.p.s.

The significant features of the spectrum of aspidocarpine are:

(1) A single sharp peak at -215 c.p.s. with area equivalent to one proton. This is attributed to the internally hydrogen-bonded phenolic OH group.

(2) A triplet with strong central peak at 44 c.p.s. This multiplet produced by the aromatic protons is of the AB type (11) with a very small chemical shift and $J = 9$ c.p.s. The total area is equivalent to two protons.

(3) A quartet at $193, 198, 202,$ and 208 c.p.s. with a total area equivalent to one proton. This is attributed to the proton at C2. The structure shows the effect of splitting by the adjacent methylene protons and demonstrates the rigidity of ring C.

(4) A single sharp peak at 211 c.p.s. of area equivalent to three protons. This is attributed to the protons of the methoxyl group.

(5) A multiplet at $247, 255, 258,$ and 263 c.p.s. of which the 258 c.p.s. peak is the strongest and sharpest. These signals are more difficult to assign to particular protons, but are probably to be associated with the protons on carbons adjacent to the nitrogen at position 9. From the area under the curve, two or at most three protons are involved with this resonance. Since ring size is known to affect the position of proton resonance in saturated heterocyclic systems (12) it would be expected that the signals of the protons at C8 would be separated from those at C10. The most likely situation is that the protons at C10 (in a five-membered ring) are involved with this multiplet while the C8 protons (in a six-membered ring) appear in the general absorption above 300 c.p.s. The sharp peak at 258 c.p.s. may be part of the C10 resonance or, if the total area does in fact represent three protons, it may be caused by the proton at C19, which is common to a five-membered and a six-membered ring and is isolated from protons which could cause splitting.

(6) A single sharp peak at 303 c.p.s. with an area equivalent to three protons. It is attributed to the protons of the N-acetyl group.

(7) A sharp peak at 400 c.p.s. with an area corresponding to about two protons, but the peak is probably associated with some of the adjacent structure and is attributed to the methyl protons of the ethyl group.

A comparison of the spectrum of aspidospermine with that of aspidocarpine shows almost all the expected relationships.

(1) The OH peak at -215 c.p.s. is absent.

(2) The aromatic protons (now three) show a multiplet of the ABC type centered on 32 c.p.s., but a complete analysis is not possible since only nine separate peaks are observed.

(3) The quartet associated with the proton at C-2 now appears at $165, 171, 175,$ and 182 c.p.s. The shift from the corresponding values in aspidocarpine is associated with the nature of the N-acetyl group. In aspidocarpine the carbonyl of this group is hydrogen-bonded with the C17 hydroxyl and this certainly pulls the oxygen away from the C2 proton. In aspidospermine, hydrogen bonding does not occur and it can readily be seen from models that the acetyl group will take up a less hindered conformation.⁶ Since a shift occurs the important deduction that can be drawn is that the assignment of the quartet to the C2 proton resonance is confirmed.

The remainder of the spectrum of aspidospermine is essentially the same as that of aspidocarpine except that the N-acetyl protons appear at 8 c.p.s. lower in the latter, an

⁶There are two less hindered conformations that can be taken up by the acetyl group. In one conformation the carbonyl and the C2—H bond have a *cis* relationship but are *trans* in the other. A *cis* relationship would cause a shift to higher frequency and since the observed shift is to lower frequency the *trans* relationship is more probable. Stereochemical predictions from scale models are in agreement with this.

effect probably produced by the hydrogen bonding with the acetyl carbonyl in aspidocarpine.

The spectrum of O-methylaspidocarpine has also given interesting information. Since the phenolic hydroxyl is blocked, hydrogen bonding is excluded in this derivative and the spectrum is very similar to that of aspidospermine except that there are two methoxyl peaks (210 and 215 c.p.s.) and the aromatic proton region shows a complete AB type (11) quartet centered on 39 c.p.s. with an area equivalent to two protons (chemical shift = 11.5 c.p.s. and $J = 8$ c.p.s.). The quartet associated with the C2 proton (166, 172, 176, 182 c.p.s.) is essentially the same as in the spectrum of aspidospermine. The relationship between the spectra in the aromatic region of aspidocarpine and O-methylaspidocarpine affords supporting evidence for the assignment on chemical grounds of substituents to positions 16 and 17. Since the oxygen function at position 17 is considered to be conclusively established, the original methoxyl group must be located at one of the three positions (14, 15, or 16). Position 15 meta to position 17 is excluded because the spectrum requires two adjacent protons. If in O-methylaspidocarpine the original methoxyl were at position 14 the protons at 15 and 16 would have almost identical environment, and a very small chemical shift would be expected. In fact the chemical shift in the O-methylaspidocarpine spectrum is greater than in the spectrum of aspidocarpine and the methoxyl must therefore be placed at position 16. The small chemical shift for the aromatic protons in aspidocarpine is explainable by the fact that the effect of a hydroxyl group on a proton para to it (i.e., at position 14) is almost the same as the effect of a methoxyl group (position 16) on a proton at its ortho position (i.e. position 15).

Conroy and his co-workers (6) have made an analysis of the spectrum of aspidospermine using a 40 Mc/s instrument, and while the major features of their spectrum correspond to those of ours (after the appropriate conversions of scale, etc.) there are several important differences. The peaks that we have assigned to the C2 and C10 protons are not easily seen in their chloroform solution spectrum, but are more evident when they used carbon tetrachloride as solvent. The peaks close to the N-acetyl and methoxyl signals which they assign to the CH_2 groups and the CH adjacent to the nitrogen do not appear in our spectrum.

EXPERIMENTAL

Melting points were determined on a Kofler micro hot stage. The infrared spectra were obtained with a Perkin-Elmer model 21 spectrophotometer, and the absorption is reported in wave numbers followed by a bracketed (m) or (s) to indicate medium or strong absorption. The ultraviolet spectra unless otherwise stated were determined with a Beckman model DU spectrophotometer.

Isolation of Aspidocarpine

The root bark of *Aspidosperma megalocarpon* Muell. Arg. (83.2 kg) was ground to a powder and percolated with petroleum ether (b.p. 95°–110°). The petroleum ether extract was concentrated under reduced pressure and the concentrate deposited the crude alkaloid in crystalline form. Aspidocarpine was purified by recrystallization from heptane and from methanol from which it separated as colorless prisms (50 g), m.p. 168.5–169.5°, $[\alpha]_D^{25} +140^\circ$ (c, 2.3 in chloroform), pK_a , 6.55 (by titration with *p*-toluenesulphonic acid). Found: C, 71.18, 71.13; H, 8.10, 8.11; N, 7.52; act. H, 0.26; CH_3CO , 10.06; C— CH_3 , 6.34; OCH_3 , 8.28, 8.29; N— CH_3 , 3.09 (spurious result); mol. equiv. 371, 374 (acid titration). Calc. for $\text{C}_{22}\text{H}_{30}\text{O}_3\text{N}_2$; C, 71.32; H, 8.16; N, 7.56; 1 act. H, 0.27;

1 CH_3CO , 11.61; 2C. CH_3 , 8.12; 1 OCH_3 , 8.38; mol. wt. 370. Infrared in chloroform: 1632, 1603, 1582 cm^{-1} , in nujol: 1637, 1605, 1587 cm^{-1} . Ultraviolet spectrum in 95% ethanol: λ_{max} , 228 $\text{m}\mu$, $\log \epsilon$ 4.42, 263.5 $\text{m}\mu$, $\log \epsilon$ 3.92, λ_{min} 249 $\text{m}\mu$, $\log \epsilon$ 3.80; after addition of a drop of aqueous sodium hydroxide: λ_{max} 224 $\text{m}\mu$, $\log \epsilon$ 4.29, 238 $\text{m}\mu$, $\log \epsilon$ 4.29, 308 $\text{m}\mu$, $\log \epsilon$ 3.65.

Aspidocarpine perchlorate, prepared in the usual manner separated from methanol as colorless needles, m.p. 280–282° (decomp.). Found: C, 56.38; H, 6.29; N, 5.93. Calc. for $\text{C}_{22}\text{H}_{30}\text{O}_3\text{N}_2 \cdot \text{HClO}_4$: C, 56.11; H, 6.64; N, 5.95%. Ultraviolet spectrum in 95% ethanol: λ_{max} 227 $\text{m}\mu$, $\log \epsilon$ 4.28, 262 $\text{m}\mu$, $\log \epsilon$ 3.82; λ_{min} 250 $\text{m}\mu$, $\log \epsilon$ 3.68.

Aspidocarpine hydrochloride crystallized from ethyl acetate–ethanol as colorless prismatic needles, m.p. 224–230° (decomp.). Found: C, 64.47; H, 7.52. Calc. for $\text{C}_{22}\text{H}_{30}\text{O}_3\text{N}_2 \cdot \text{HCl}$: C, 64.93; H, 7.63%.

The hydrobromide separated from methanol as prismatic needles m.p. 288–290°. Found: C, 57.82; H, 6.68. Calc. for $\text{C}_{22}\text{H}_{30}\text{O}_3\text{N}_2 \cdot \text{HBr} \cdot 0.5\text{H}_2\text{O}$: C, 57.38; H, 7.00%.

Aspidocarpine hydriodide crystallized in rectangular plates from methanol, m.p. 272–274° (decomp.). Found: C, 52.17; H, 6.09. Calc. for $\text{C}_{22}\text{H}_{30}\text{O}_3\text{N}_2 \cdot \text{HI} \cdot 0.5\text{H}_2\text{O}$: C, 52.08; H, 6.35%.

O-Acetylaspidoarpine

Aspidocarpine (281 mg) was dissolved in acetic anhydride (3 ml) containing pyridine (0.8 ml) and allowed to stand at room temperature for 6 hours. The solution was evaporated to dryness under reduced pressure, the residue dissolved in benzene and chromatographed on neutral alumina. Careful elution with benzene and evaporation of the eluate gave a crystalline product which separated from hexane–ether as colorless prisms, m.p. 165–167°, $[\alpha]_D^{25} -8.4^\circ$ (*c*, 0.81 in chloroform). Found: C, 69.90; H, 7.78; CH_3CO , 20.25. Calc. for $\text{C}_{24}\text{H}_{32}\text{O}_4\text{N}_2$: C, 69.88; H, 7.82; CH_3CO (one OAc + one NAc) 20.86%. Infrared in chloroform: 1768 (s), 1666 (s) cm^{-1} . Ultraviolet (95% ethanol; Cary model 11M): λ_{max} ($\log \epsilon$) 223 $\text{m}\mu$ (4.53), 253 $\text{m}\mu$ (3.98), 292 $\text{m}\mu$ (3.61); λ_{min} ($\log \epsilon$), 240 $\text{m}\mu$ (3.89), 272 $\text{m}\mu$ (3.28). The spectrum was not appreciably affected by the presence of base.

O-Methylaspidoarpine

Aspidocarpine (1.040 g) was dissolved in dilute hydrochloric acid (20 ml) and the solution made basic by the cautious addition with stirring of 20% aqueous sodium hydroxide. A precipitate was first formed which redissolved after the solution had become basic. Methylation was carried out with methyl sulphate (5 ml) in the usual manner. The product which separated as the reaction proceeded was filtered off and washed with water. After two crystallizations from aqueous methanol it consisted of prismatic needles (0.752 g) m.p. 152–154° $[\alpha]_D^{25} -94^\circ$ (*c*, 1.15 in chloroform). Found: C, 71.44; H, 8.10; CH_3O , 16.58; CH_3N , 0.94 (spurious). Calc. for $\text{C}_{23}\text{H}_{32}\text{O}_3\text{N}_2$: C, 71.84; H, 8.39; 2 CH_3O , 16.14%. pK_a 6.9 (titration with *p*-toluenesulphonic acid in 50% ethanol).

Infrared (chloroform): 1660 (sh), 1645 (s) cm^{-1} ; in carbon tetrachloride, 1663 (s) cm^{-1} ; in nujol, 1656 (s) cm^{-1} . Ultraviolet in 95% ethanol: λ_{max} ($\log \epsilon$) 224 $\text{m}\mu$ (4.60), 252 $\text{m}\mu$ (4.07), 288 $\text{m}\mu$ (3.44), λ_{min} ($\log \epsilon$), 244 $\text{m}\mu$ (4.03), 279 $\text{m}\mu$ (3.41). The spectrum was not appreciably affected by base.

O-Methyldeacetylaspidoarpine

O-Methylaspidoarpine (107 mg) was dissolved in 10% hydrochloric acid (5 ml) and the solution refluxed in an atmosphere of nitrogen for 3 hours. The cooled solution was

made basic with solid sodium carbonate and immediately extracted with chloroform. After drying (sodium sulphate) the extract was evaporated to dryness and the residue dissolved in aqueous methanol from which it crystallized as white needles (50 mg), m.p. 151–152°. Recrystallization raised the melting point to 153–154°. $[\alpha]_D^{25} -4.9^\circ$ (*c*, 1.03 in chloroform). pK_a 7.8 (titration with *p*-toluenesulphonic acid in 50% ethanol). Found: C, 73.95; H, 8.83; N, 8.65. Calc. for $C_{21}H_{30}O_2N_2$: C, 73.64; H, 8.83; N, 8.18%. Infrared in nujol 3335 cm^{-1} . Ultraviolet in 95% ethanol: strong end absorption, λ_{inf} 240 $m\mu$, $\log \epsilon$ 3.82, λ_{min} 268 $m\mu$, $\log \epsilon$ 2.97; λ_{max} 293 $m\mu$, $\log \epsilon$ 3.49. The spectrum was not appreciably affected by acid.

Treatment of a sample of O-methyldeacetylaspido carpine with acetic anhydride and pyridine reconverted it to O-methylaspido carpine in about 50% yield.

O,O-Diacetyl-O-demethylaspido carpine

Aspidocarpine (731 mg) was refluxed with constant boiling hydrobromic acid (10 ml) in an atmosphere of nitrogen for 1 hour. The solution was evaporated to dryness under reduced pressure and the residue heated on the steam bath with acetic anhydride (15 ml) in an atmosphere of nitrogen for 3 hours. The solution was evaporated to dryness under reduced pressure and the residue dissolved in dilute aqueous sodium carbonate. This solution was extracted with ether and the extract washed with a little water and dried (sodium sulphate). Evaporation of the ether yielded a residue (757 mg) which crystallized from hexane-acetone as yellowish microcrystals (510 mg), m.p. 140–144°. After treatment with charcoal and recrystallization from the same solvent, the product consisted of colorless platelets, m.p. 144–145°, $[\alpha]_D^{25} +9.8^\circ$ (*c*, 1.33 in chloroform). Found: C, 68.21; H, 7.19; CH_3CO , 30.36. Calc. for $C_{26}H_{32}O_5N_2$: C, 68.16; H, 7.32; $3CH_3CO$, 29.31%. Infrared in chloroform: 1777 (sh), 1767 (s), 1668 (s) cm^{-1} (in nujol, 1204 cm^{-1}).

O-Demethylaspido carpine

The material was prepared first by controlled hydrolysis of *O,O*-diacetyl-*O*-demethylaspido carpine but it was found more convenient to start with aspidocarpine and carry out the whole preparation in the same flask without isolating the intermediates in pure form.

Aspidocarpine (1.043 g) was treated successively with hydrobromic acid and acetic anhydride as described above for the preparation of the diacetyl derivative. After removal of the acetic anhydride, the crude residue was dissolved in methanol (25 ml) to which was added 20% aqueous sodium hydroxide (2.5 ml). The solution was refluxed in an atmosphere of nitrogen for 20 minutes and then evaporated under reduced pressure to a volume of about five milliliters. Crushed ice (ca. 5 g) was added, the solution made just acid with 5% sulphuric acid, then brought to pH 8 with aqueous sodium carbonate and finally thoroughly extracted with chloroform. The extract was dried (sodium sulphate) and the solvent removed by evaporation. The residue, a brown solid (0.845 g) was dissolved in a mixture of ether and benzene and passed through a short column of silica gel which was then eluted with a mixture of benzene (4 parts) and ether (1 part). Evaporation of the eluate yielded a colorless solid (0.676 g) which, on crystallization from aqueous methanol, formed needles, m.p. 130° with an apparent phase change and partial melting at 92–94°. Recrystallization from benzene produced colorless tablets, m.p. 130°, with softening above 125°. After drying *in vacuo*, found: C, 70.91; H, 8.17; N, 7.79. Calc. for $C_{21}H_{28}O_3N_2$: C, 70.76; H, 7.92; N, 7.86%. $[\alpha]_D^{25} +121^\circ$ (*c*, 0.81 in chloroform). Infrared (nujol), 3330 (m), 1634 (s) cm^{-1} . Ultraviolet (pure ethanol): λ_{max} ($\log \epsilon$) 227 $m\mu$ (4.41),

262 $m\mu$ (4.01), λ_{min} (log ϵ) 248 $m\mu$ (3.86). In the presence of buffered boric acid: strong end absorption, λ_{inf} (log ϵ) 258 $m\mu$ (4.08), λ_{max} (log ϵ) 290 $m\mu$ (3.56).

For the determination of the ultraviolet spectra in the presence of buffered boric acid a stock solution of O-demethylaspidocarpine (2.0 mg) in pure ethanol (10 ml) was prepared. Simple dilution of the stock solution afforded the solution used in determining the spectrum of the untreated substance. For the spectrum in the presence of buffered boric acid, the stock solution (1 ml) was added to a saturated solution of boric acid in ethanol (2 ml) and diluted to 10 ml with ethanol. Excess anhydrous sodium acetate was added, and the mixture was thoroughly shaken and allowed to stand for 20 minutes before use.

Treatment of O-demethylaspidocarpine in methanol with an ethereal solution of diazomethane reconverted it to aspidocarpine in 60% yield.

Aspidocarpine-N(b)-methiodide

Aspidocarpine (258 mg) was dissolved in dimethylformamide (5 ml) containing methyl iodide (3 ml) and heated under reflux on a steam bath for 4 hours. The solution was evaporated to dryness on a rotary evaporator and the yellow residue crystallized from methanol from which it separated as yellowish crystals (170 mg), m.p. 280–284° (decomp.). Recrystallization from the same solvent gave colorless rectangular plates, m.p. 288–290° (decomp.). Found: C, 52.93; H, 6.26. Calc. for $C_{22}H_{30}O_3N_2 \cdot CH_3I \cdot 0.5H_2O$: C, 52.98; H, 6.57%.

Aspidocarpine-N(b)-methiodide (34 mg) was refluxed for 30 minutes with a solution of potassium hydroxide (70 mg) in 95% ethanol (5 ml) in an atmosphere of nitrogen. The solution was evaporated to dryness under reduced pressure and the yellowish residue dissolved in water (5 ml). The aqueous solution was thoroughly extracted with ether, the extract washed with a little water, dried (sodium sulphate), and evaporated to dryness. The residue was a slightly discolored crystalline solid (17 mg) which, on recrystallization, proved identical with an authentic sample of aspidocarpine.

von Braun Degradation: Aspidocarpine Bromocyanamide

Aspidocarpine (215 mg) was refluxed with cyanogen bromide (416 mg) in chloroform (10 ml) for 24 hours. Evaporation of the solution left a white residue which was triturated with ethyl acetate. The insoluble fraction (70 mg) proved to be aspidocarpine hydrobromide. The ethyl acetate solution when concentrated deposited a colorless crystalline solid (133 mg), m.p. 167–169°, which formed needles, m.p. 170–171° on recrystallization from methanol. Found: C, 58.45; H, 6.33; N, 8.93. Calc. for $C_{23}H_{30}O_3N_3Br$: C, 57.98; H, 6.35; N, 8.81%. Infrared (nujol): 2218(m), 1633(s) cm^{-1} .

In a subsequent preparation, the alkaloid hydrobromide was removed by dissolving the crude mixture in chloroform and chromatography on a short column of neutral alumina.

Aspidocarpine bromocyanamide (73 mg) was refluxed for 6 hours with 95% ethanol (9 ml) in an atmosphere of nitrogen. The solution was concentrated to a small volume under reduced pressure, diluted with a little water, made basic with solid sodium carbonate, and extracted with chloroform. The extract, after drying over sodium sulphate, was chromatographed on a short column of neutral alumina and eluted with chloroform. The eluate yielded a solid product (60 mg) which, on crystallization from methanol, formed colorless prisms identical in every respect with aspidocarpine.

Chromic Acid Oxidation

(a) *Aspidocarpine*

The alkaloid (1.131 g) was dissolved in water (17 ml) containing sulphuric acid (3 ml) and heated on a steam bath. Chromium trioxide (1.8 g) dissolved in a little water was cautiously added over a period of about one hour. Heating was continued for a further hour and the hot solution subsequently made basic with hot aqueous barium hydroxide and filtered. The yellow filtrate was exhaustively extracted with chloroform and the dried (sodium sulphate) extract evaporated. A semisolid residue was left (0.169 g) which was dissolved in benzene, chromatographed on neutral alumina, and crystallized in a mixture of hexane and acetone from which it separated as yellowish microcrystals (76 mg), m.p. 222–224°. Recrystallization from the same solvent gave pale yellowish rods, m.p. 224–225°, $[\alpha]_D^{25} -132^\circ$ (c, 1.03 in chloroform). Found: C, 68.87; H, 8.52; N, 10.63. Calc. for $C_{15}H_{22}O_2N_2$: C, 68.67; H, 8.45; N, 10.68%. Infrared (chloroform): 3410 (w), 1762 (s), 1728 (vs) cm^{-1} . Ultraviolet (95% ethanol): λ_{min} 227 m μ log ϵ 3.31, λ_{max} 252 m μ log ϵ 3.55, 336 m μ , ϵ 59. In the presence of a drop of dilute aqueous potassium hydroxide: λ_{min} 234 m μ log ϵ 3.28, λ_{max} 268 m μ log ϵ 3.48 (longer wave-length absorption not measured).

(b) *Aspidospermine*

Aspidospermine obtained from Inland Alkaloid Co., and recrystallized (1.020 g) was treated with chromic acid as described above, except that heating was continued for 8 hours. The crude product (0.105 g) proved more difficult to purify than the oxidation product of aspidocarpine. The crystalline product, m.p. 223–225°, has $[\alpha]_D^{25} -128^\circ$ (c, 0.47 in chloroform). Its infrared spectrum contained the same peaks as that of the oxidation product of aspidocarpine and the X-ray diffraction patterns of both compounds were identical.

ACKNOWLEDGMENTS

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THE ELECTROCHEMICAL BEHAVIOR OF THE NICKEL OXIDE ELECTRODE

PART II. QUASI-EQUILIBRIUM BEHAVIOR¹

P. L. BOURGAULT AND B. E. CONWAY

ABSTRACT

The electrode potential of the nickel oxide electrode has been determined as a function of water and solute activity in aqueous solutions of potassium hydroxide. The electrode, which was charged to a mean state of oxidation corresponding to 50% Ni II and 50% Ni III, was examined after long periods of time and by cathodic and anodic e.m.f. decay measurements after polarization in order to establish the quasi-reversible potentials by two methods. The results are discussed in terms of the stoichiometry of the potential-determining reaction, and distinction between mixed and true reversible potentials is made.

INTRODUCTION

We have previously examined in part I (1) the kinetic behavior of the "overcharged" nickel oxide electrode with regard to rates of self-discharge and oxygen evolution. In the present paper we present data on the quasi-equilibrium potentials of the nickel oxide electrode in aqueous potassium hydroxide solutions. The behavior of the electrodes is referred to as "quasi-equilibrium" since the electrodes are continuously losing charge on open-circuit by the corrosion type of process described previously (1).

This can affect the electrode in two ways: firstly to produce a continuous but slow decrease of the state of oxidation of the oxide and secondly to give rise to an electrode potential which is more cathodic than the true equilibrium potential corresponding to the formal state of oxidation of the oxide. In fact, the potentials measured on open-circuit are analogous to mixed potentials observed in corrosion, since there is a slow anodic evolution of oxygen and a corresponding cathodic self-reduction of the oxide. This factor does not seem to have been realized in previous work (2, 3, 4). However, by suitable choice of conditions and methods of study it is possible to determine the potential of the electrode under conditions very near to equilibrium. Thus, if the electrodes are left in dilute potassium hydroxide (0.001 *M*) for several days, the potential ceases to change by more than 0.1 mv per hour and the potential of the electrode may then be examined as a function of potassium hydroxide activity without further significant self-discharge during the measurements. Also in the solutions of higher alkali concentration the electrode is more stable* since the open-circuit potential becomes less anodic to the reversible oxygen potential and the rate of self-discharge (already allowed to become small in the 0.001 *M* solution) becomes negligible.

Electrode potentials and stoichiometric reactions for the potential-determining reaction at the nickel oxide electrode have been discussed in earlier work by Forster (2) and Zedner (3) and more recently by Kornfeil (4). A potential of 0.49 v has been attributed to the nickel oxide electrode by Latimer (5), but no evidence that the potential-determining species (e.g. NiO₂) are those written by Latimer (5) has been given; in fact there is no evidence that NiO₂ exists as such in the electrochemically active material in the nickel

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Contribution from the Department of Chemistry, University of Ottawa, Ottawa, Ontario.

*This is not in contradiction to our previous findings (1); in the latter work we showed that the exchange currents for oxygen evolution became greater in the solutions of higher alkali concentration. In the present work the open-circuit potentials are lower in the stronger solutions so that the oxygen "overpotential" is relatively smaller and the self-discharge rate is hence less at the open-circuit potential.

oxide electrode. The IV-valent state of nickel may exist in a non-stoichiometric oxide lattice in electrodes charged beyond the " $\text{NiO}_{1.5}$ " composition but it is not possible at room temperature to achieve states of oxidation greater than about " $\text{NiO}_{1.7}$ " (6), so that the oxide cannot be completely oxidized to the " NiO_2 " state. In other work (2, 3) the stoichiometric reactions suggested are not in mutual agreement and the more recent work (4) contributes further serious discrepancies.

We have therefore examined the potential of partially charged nickel oxide electrodes at a controlled formal state of oxidation as a function of potassium hydroxide and water activity in aqueous alkali solutions by a polarization decay method in which the reversible potential is approached both from the anodic and cathodic directions. This method may be expected to give more reliable values of the electrode potential than those obtained by leaving the electrode on open-circuit for arbitrary periods of time. We have also compared data obtained by the decay method with the e.m.f. values from "stationary" potential measurements i.e. at very long times, and deduced the nature of the potentials which are measured by these procedures. From these determinations, the role of potassium hydroxide and water in the over-all potential-determining reaction can be evaluated.

EXPERIMENTAL

1. General

Nickel hydroxide electrodes were prepared in nickel sinters as described previously and charged anodically (7, 1) to the higher oxide for 30 hours at 25°C in aqueous potassium hydroxide (analytical grade) solutions of the concentrations indicated below, until an appreciable rate of oxygen evolution was maintained.

2. Reversible Potentials from Polarization Decay Measurements

Here the potentials of nickel oxide electrodes at a formal state of oxidation of $\text{NiO}_{1.25}$ were determined by extrapolating cathodic and anodic e.m.f. decay lines, plotted logarithmically in time, to the potential of their intersection. This procedure is analogous to the determination of reversible potentials by extrapolation of anodic and cathodic Tafel lines to zero overpotential (cf. 26).

The electrodes were prepared as described above and initially charged in solutions of KOH of various concentrations at 38.2 ma per gram of $\text{Ni}(\text{OH})_2$ for 30 hours at 25°C . The electrodes were then left to stand on open-circuit to allow the surface pseudocapacity (8) to become discharged. The remaining bulk electrochemical capacity* was then determined by discharging the electrode at a constant rate such that the theoretical capacity (based on a state of oxidation " $\text{NiO}_{1.5}$ ") would be discharged in 5 hours. The observed charge held by the electrodes agreed with that expected theoretically to within 10% (this deviation simply means that a state of oxidation slightly different from $\text{NiO}_{1.5}$ is reached initially). On the basis of this determination, a charging rate i_c was then chosen such that the electrode would be oxidized to 50% $\text{Ni}^{\text{II}}\text{--Ni}^{\text{III}}$ (i.e. $\text{NiO}_{1.25}$) in 1 hour. The charging was interrupted and the decay of potential was followed on open-circuit for 24 hours or more on a recording potentiometer. The charging was resumed at the rate i_c for 2 hours; after decay on open-circuit for several hours (to again discharge the surface capacity associated with oxygen evolution), discharging was commenced at the rate $-i_c$ for 1 hour so that the electrode regained a state of oxidation of " $\text{NiO}_{1.25}$ ". The discharging current was interrupted and the potential decay from this cathodic

*We use the term "capacity" here in the sense familiar in battery technology. We in fact determine the Faradaic charge, which can be withdrawn from the electrode by the current i_c passing for a measured period of time.

polarization was followed for 24 hours, after which the remaining bulk electrochemical "capacity" was checked by complete discharge with the same current, $-i_0$.

This sequence of operations and the corresponding e.m.f.'s are shown schematically for a typical experiment (in 7.3 *M* KOH) in Fig. 1.

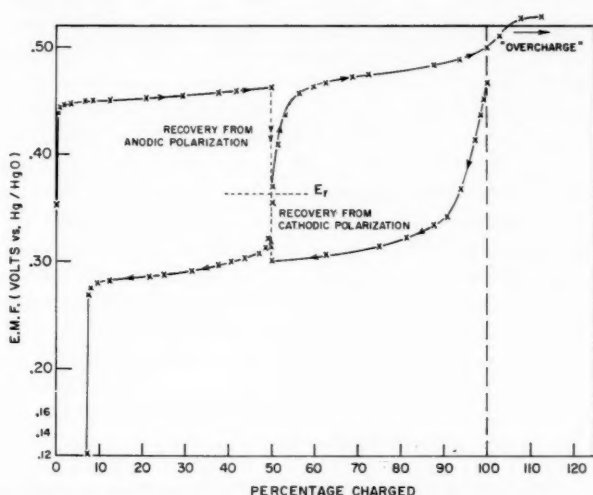


FIG. 1. Charging and discharging cycle for the nickel oxide electrode used in polarization decay studies.

3. Quasi-Equilibrium Potentials

In this series of measurements, electrodes were allowed to stand on open-circuit in 0.001 *M* aqueous KOH until the degree of charge corresponded to an approximate state of oxidation of "NiO_{1.25}". The electrodes were then transferred to other potassium hydroxide solutions by the following three alternative procedures:

(a) Six electrodes were transferred directly into solutions 14.6, 11.0, 7.3, 3.7, 1.46, and 0.146 *M* in KOH, respectively, which were stirred by bubbling purified oxygen. The e.m.f. of the electrodes was followed as a function of time (versus a Hg/HgO electrode) for 1 week.

(b) Six electrodes were transferred from the 0.001 *M* KOH to a solution of 14.6 *M* KOH where they were allowed to stand for about 24 hours; they were then transferred to solutions of 0.07, 0.146, 0.73, 1.46, 7.3, and 11 *M* KOH respectively and again the e.m.f. was recorded at regular intervals of time.

(c) (i) An electrode was taken from the 0.001 *M* KOH solution and then allowed successively to equilibrate in 0.07, 0.7, 3.65, 7.3, 11.0, and 14.6 *M* KOH solutions for periods of 2 hours during which the e.m.f. became constant to better than 0.5 mv per hour. A reverse series of measurements was then made by transferring the electrodes back from the concentrated to the more dilute solutions.

(ii) A similar series of e.m.f. values were obtained by transferring the electrode from the 0.001 *M* KOH directly to the strongest (14.6 *M*) solution and thence successively to the more dilute solutions and back again to the more concentrated ones.

From these measurements, the reversibility of the e.m.f. changes with changes of

concentration could be judged. The sequence of changes of conditions and corresponding e.m.f. values can be seen by reference to Fig. 2.

The degree of oxidation of the electrodes was measured after the e.m.f. runs by discharging the electrodes at a controlled current (30 ma per gram of $\text{Ni}(\text{OH})_2$) and hence determining coulometrically their electrochemical "capacity".

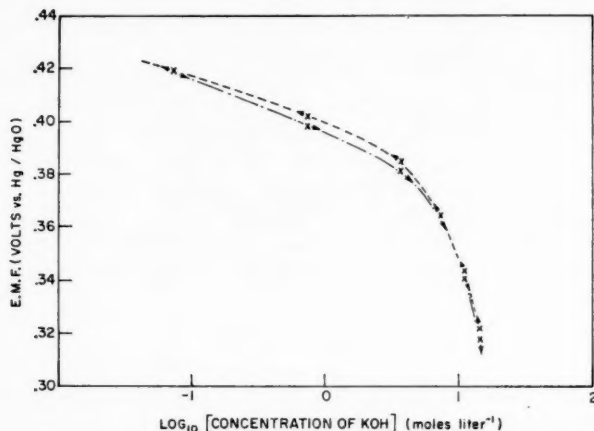


FIG. 2. Reversibility of e.m.f. of the nickel oxide electrode with successive changes of concentration. Arrows indicate sequence of changes for electrode initially put in strongest solution after being maintained in 0.001 M KOH.

4. Solutions

Aqueous solutions of analytical grade potassium hydroxide were made up by diluting a saturated (25° C) solution of potassium hydroxide kept in a "seasoned" closed "polythene" bottle. Concentrations were checked after runs by titration against standard acid. The water used had been prepared from distilled water by a further distillation from alkaline permanganate in a still provided with three glass spray traps. Use of potassium hydroxide recrystallized at -20° C gave results insignificantly different from those obtained with the analytical grade reagent.

Several experiments were also carried out in heavy water (99.76% D_2O) and in these cases, KOD solutions in D_2O were prepared by decomposing electrolytically prepared dry potassium amalgam with the heavy water. The nickel oxide electrodes for this part of the work were prepared by impregnating the sinters with a solution of nickel sulphate made up from the anhydrous substance by dissolution in deuterium oxide. The Ni_2SO_4 was obtained from the hexahydrate by heating it to constant weight (52 hours) at 600–700° C. Control runs were also carried out on electrodes prepared by the same method but using ordinary water as the solvent.

5. Measurement of e.m.f.

Potentials of the nickel oxide electrodes were measured against yellow mercuric oxide electrodes (9) in the same solutions by means of a Tinsley potentiometer and a Philips high input impedance recording potentiometer capable of measuring to 0.5 mv on a full scale of 100 mv on various voltage ranges.

RESULTS

1. Polarization Decay

The kinetic significance of measurements of decay of e.m.f. after cessation of a polarization has been treated previously (10, 11). Thus, the rate of decay of e.m.f. with (Naperian) logarithmic time gives the Tafel slope $-RT/\alpha F$ for the rate-determining mechanism involved in the discharge of the double-layer or surface capacity provided that this capacity is constant in the range of potentials over which the polarization decay occurs. At very long times of decay, the e.m.f. approaches the reversible potential asymptotically as discussed previously (11). Thus, plots of e.m.f. during decay from both anodic and cathodic polarization vs. the logarithm of the effective time of decay can be extrapolated to a potential where they intersect and this potential should approximate closely to the reversible potential E_r (unless other alternative processes can occur), which would theoretically be reached only after infinite time. Plots of decay of anodic and cathodic polarization as a function of time t plus θ , where θ is the semiempirical constant discussed previously (11, 1), are shown for the $\text{NiO}_{1.25}$ electrode in Figs. 3a-d and 4a, b for the indicated concentrations of potassium hydroxide. The quantity θ can be regarded as the time required for the potential of the electrode to fall from an infinite value to that at the commencement of decay of the polarization corresponding to passage of a current i_c . The constant θ is given by

$$[1] \quad \theta = Cb/2.3 i_c$$

where b is the Briggsian slope for the decay process and C is the capacity suffering discharge by the electrochemical process. The quantity θ is determined as described previously (1, 11) by an empirical procedure but is not involved in the kinetic equations determining the slope b and hence the extrapolated values of E_r .

In order to establish the effect of varying water activity at a constant KOH activity, one experiment was carried out in a saturated aqueous KF solution (25°C) 0.08 molar (i.e. approximately unit activity (see Discussion, Section 4)) in KOH. The anodic and cathodic decay lines are shown in Fig. 4b.

In the Figs. 3a-d and 4a, b, the extrapolated values of potential designated E_m or E_r (see below) are shown in the brackets on the ordinate axes and are indicated by dotted lines. Cases where inflections occur in the anodic lines are discussed in detail below.

Decay lines similar to those in Figs. 3a-d and 4a, b are also given in Fig. 5 for the nickel oxide electrodes in a 0.93 *M* KOD solution in deuterium oxide and the data shown are the means of two sets of values which agreed to ca. ± 2 mv.

2. Quasi-Equilibrium Potentials

The potentials obtained by the procedure *c(ii)* described in Section 3 under Experimental are shown as a logarithmic function of molar concentration of KOH in Fig. 2. The results obtained from "backward" successive immersions agreed with those obtained by "forward" immersions as shown in this figure but some irreversibility occurs when the sequence of operations is carried out by immersing the electrode initially in dilute solutions (*c(i)*) followed successively by more concentrated solutions and then returned to the more dilute solutions. These values obtained in the "forward" direction by procedure *c(i)* are not therefore regarded as true equilibrium values.

In Fig. 6, comparison is made between the data obtained by procedure *b* (crosses)

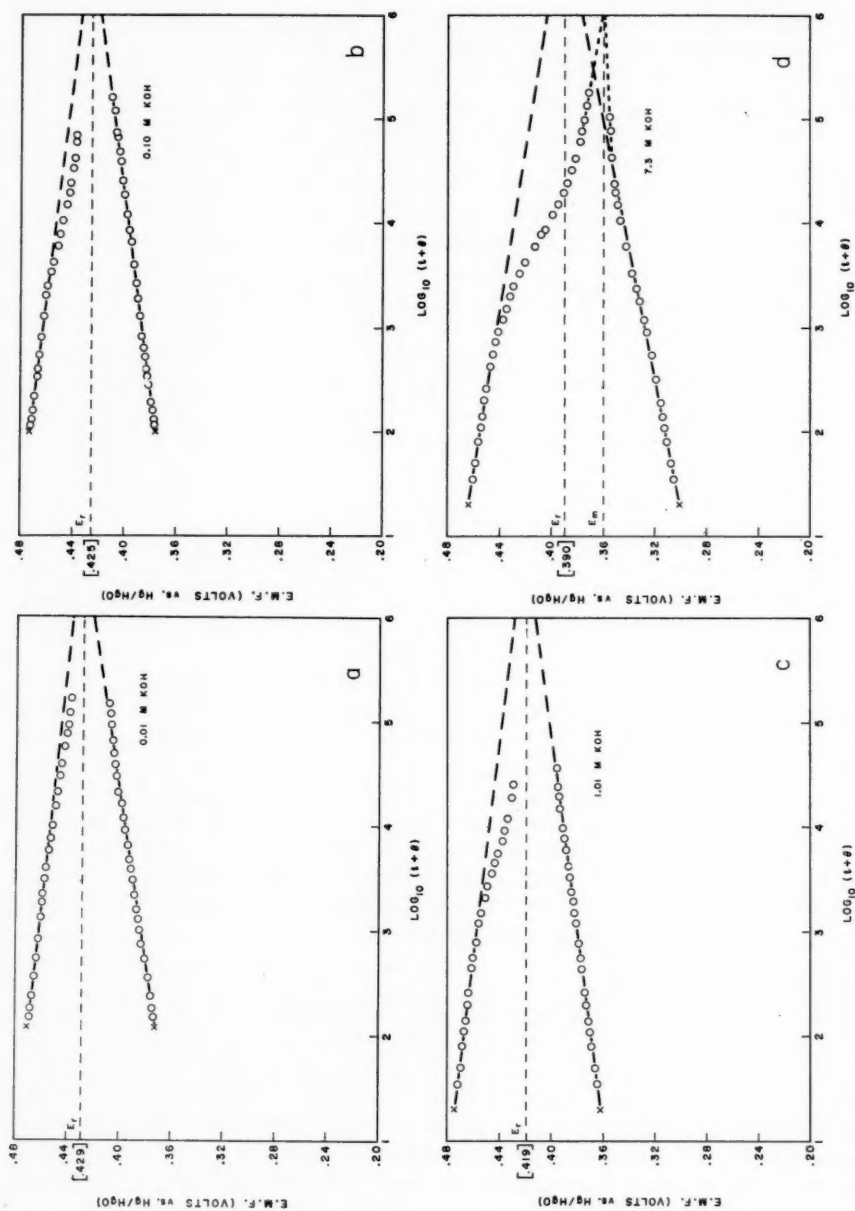


FIG. 3. Decay of e.m.f. from anodic and cathodic polarization as a logarithmic function of effective time of decay. (a) 0.01 M KOH; (b) 0.10 M KOH; (c) 1.01 M KOH; (d) 7.3 M KOH.

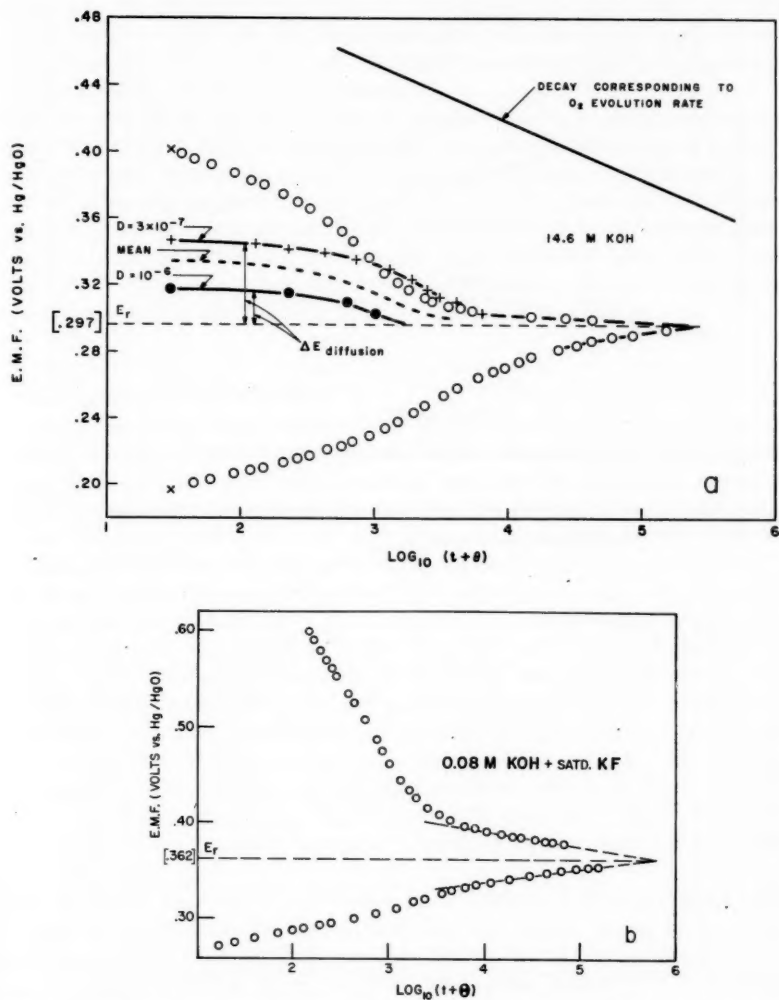


FIG. 4. Decay of e.m.f. from anodic and cathodic polarization as a logarithmic function of effective time of decay.

(a) 14.6 M KOH showing decay of concentration polarization, $\Delta E_{\text{diffusion}}$, and decay rate corresponding to rate of oxygen evolution.

(b) Saturated KF + 0.08 M KOH.

(taking the e.m.f. attained 24 hours* after transfer of an electrode from a strong solution to a more dilute one) and the polarization decay method (circles) and it is seen that the polarization decay values tend to be significantly more positive (ca. 15–30 mv) to the Hg/HgO electrode than those obtained by procedure *b*. This is in fact to be expected

*The e.m.f. values obtained by procedure *c* are not used for comparison with the decay values since the times of equilibration may have been too short for electrolyte diffusion effects to have become negligible in the strongest solutions (see Appendix).

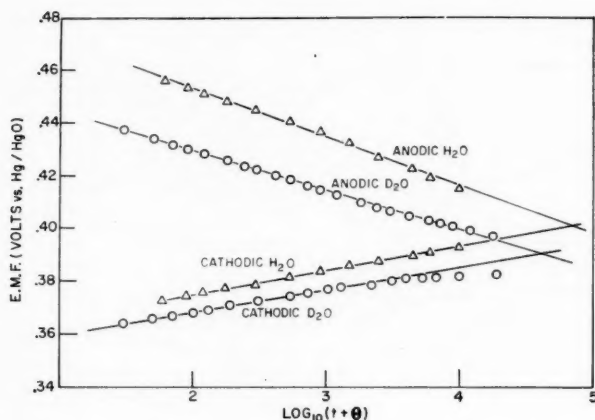


FIG. 5. Decay of e.m.f. from anodic and cathodic polarization in 0.93 *M* KOD/D₂O or KOH/H₂O.

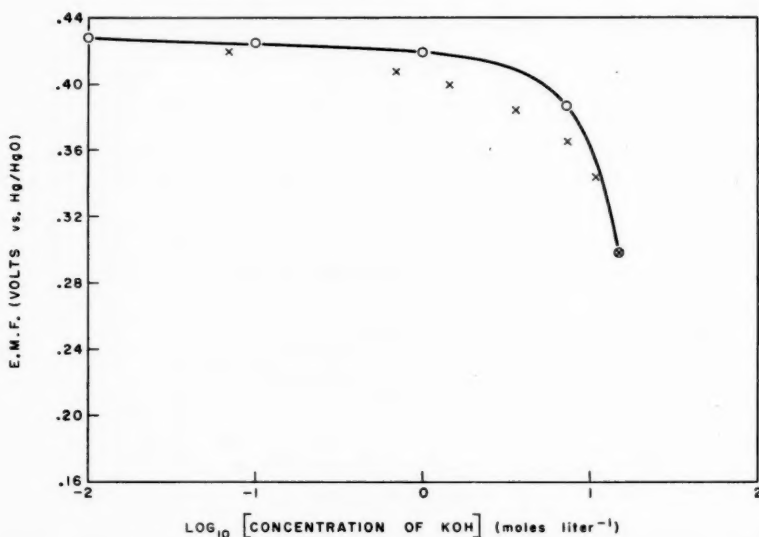


FIG. 6. Comparison of e.m.f. values obtained from "stationary" potential measurements (crosses) and from appropriate extrapolation of logarithmic decay lines (circles).

since the values obtained by the latter procedure are the mixed potentials and will be depressed from the true reversible potential by the small cathodic polarization impressed on the electrode by virtue of its finite rate of self-discharge by the corrosion-type of process discussed previously (1).

3. Accuracy and Reproducibility

Owing to kinetic self-discharge effects and to the relatively complex method (7, and above) of preparation of the electrodes at a controlled state of charge, reproducibility of

electrode potentials cannot be expected to be so good as that obtainable with primary standard half-cells, e.g. the Ag/AgCl electrode (12). However, replicate runs usually gave e.m.f. values (vs. the Hg/HgO electrode) reproducible to ± 3 mv from either the polarization decay method or the procedure *b*.

The precision of the measurements was greater than this since potentials measured on the Tinsley and automatic recording potentiometers could be read to 0.2 mv and 0.5 mv, respectively, with a similar accuracy after standardization by means of a Weston cadmium cell. The temperature of the air thermostat used to house the cells during measurements was constant to $\pm 0.1^\circ$ C. The order of magnitude of the temperature coefficient of the e.m.f. of the nickel oxide-mercuric oxide electrode pair is 10^{-1} mv $^\circ\text{C}^{-1}$ (13) so that the constancy of temperature provided was more than adequate to ensure insignificant errors of e.m.f. arising from temperature fluctuations.

DISCUSSION

1. Nature of the Electrode Processes

In the polarization decay studies, the aim was to disturb the equilibrium between reduced and oxidized forms of the nickel oxide in the semicharged electrode (" $\text{NiO}_{1.25}$ ") by passing an anodic or a cathodic current and then observing the decay towards the reversible potential of the oxide electrode. However, whilst passage of a current in either direction will cause a change in the formal degree of oxidation of the bulk material, for the reasons given below this process is found to be an *indirect* one.

The quantity θ , which can be determined empirically for the decay lines shown in Figs. 3 and 4, as described previously (11, 1), enables the surface capacity associated with the electrochemical processes involved in the decay of e.m.f. to be calculated (equation [1]) and the values found are between 500 (7 *M* KOH) and 3000 (0.01 *M* KOH) farads per gram of $\text{Ni}(\text{OH})_2$. This capacity is very much larger by several orders of magnitude than any possible ionic double-layer capacity corresponding to the real area of the nickel in the sinter (5000 cm^2 * in an electrode capable of supporting 1 g of $\text{Ni}(\text{OH})_2$). On the other hand, the charge which can be withdrawn from this capacity over a given voltage range is very much smaller, by a factor of 50–100, than that which can be withdrawn as conventional electrochemical "capacity" from the bulk material over a comparable range of voltage.

The values of the capacity obtained from θ were checked by observations on the potential (*E*)-time (*t*) relations for build-up and forced decay of e.m.f. at constant current using the half-charged electrodes. Although there was some hysteresis between build-up and forced decay lines, the mean capacities obtained as $d(it)/dE$ from these measurements were comparable with the capacity values obtained from θ .

The above values of capacity must therefore be regarded as corresponding to a *surface* layer (14a) of intermediates (probably adsorbed radicals of OH or O) which participate in the process of oxidation of the bulk material. Conversely, the reduction of the bulk material proceeds by an opposite process, and the reactions observed in the cathodic and anodic polarization and their decay correspond, respectively, to removal and formation of this surface layer. The capacity associated with this layer may be referred to as a "surface capacity" in which the degree of charge must be changed before any chemical changes in the bulk oxide can be effected.

We may therefore qualitatively represent the behavior of the electrode upon charge or

*This value was kindly determined by Dr. C. Amberg of the National Research Council on an outgassed sample of sinter by the B.E.T. method.

discharge by the electrical analogue shown in Fig. 7 where C_s is the surface capacity, C_B that corresponding to the electrochemically active bulk material, R_{O_2} the non-ohmic

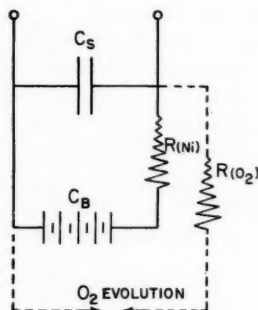


FIG. 7. Schematic equivalent circuit by which charging and discharging of electrode can be represented.

resistance corresponding to the reciprocal of the rate of electrochemical oxygen evolution, and R_{Ni} that corresponding to the reciprocal of the rate of oxidation or reduction of the bulk material by the chemisorbed species constituting the surface pseudocapacity.

When current is made to flow anodically into the system through the two schematic terminals at the top of the circuit (Fig. 7), C_s is first charged up and in the steady state, charge flows mainly through R_{Ni} with some "leakage" through R_{O_2} , giving, respectively, simultaneous oxidation of the bulk material (C_B) and some oxygen evolution. On open-circuit, following anodic polarization, oxygen evolution still occurs (but this can only be detected in the "over-charge" region (Fig. 1) as described previously (1)) and the remainder of the excess charge on C_s passes into C_B with resultant oxidation of the material. This indirect mechanism of charging is supported by the direction of the H/D isotope effect on the polarization on charging and discharging (Fig. 5), which is significantly *less* in D_2O than in H_2O . If H^+ or D^+ transfer steps (1, 6) were rate-determining in the oxidation or reduction of the bulk oxide the reverse isotope effect would be expected (20). The *faster* rate in D_2O is connected with the expected lower heat of solvation of OD^- than that of OH^- in the respective isotopic solvents (21).

Conversely, on cathodic polarization, C_s is discharged to potentials low enough for current to flow from C_B through R_{Ni} sufficient to maintain the current taken from the over-all system, the oxygen evolution rate then being negligible at these more cathodic potentials (it becomes significant in some cases only as the reversible or mixed potential is reached, e.g. in Fig. 3d). On open-circuit following cathodic polarization, C_s can be regarded as recharged by the current through R_{Ni} (less the small current corresponding to oxygen evolution) and this corresponds to the lower recovery lines shown in the Figs. 3a-d and 4a.

At long times after cessation of anodic or cathodic polarization, the potential across C_s would become equal to that set up across C_B if no leakage occurred through R_{O_2} , i.e. if no self-discharge were taking place, and the reversible potential of the electrochemically active material constituting C_B would then be measured by the potential at which the extrapolated logarithmic decay lines intersect. Inspection of the e.m.f. decay lines indicates, however, that in all but the most dilute solutions there are inflections in the anodic lines and at the highest concentrations (14.6 M) also in the cathodic line. This

raises the problem of how the extrapolations should be carried out, i.e. by extension of the upper lines in the region of low times (i.e. $\log [t+\theta]$ in the range 1 to 3) or production of the lines after the longest periods of time (i.e. for $\log [t+\theta] > 4$). We therefore now consider possible reasons for these inflections in the decay lines.

2. Form of the Decay Lines

(a) Oxygen Evolution Rates

The anodic decay lines for concentrations greater than 0.1 *M* KOH show an inflection from a low slope to a high slope with increasing time which is characteristic of alternative electrochemical reactions with different Tafel slopes as discussed by Parsons (14). From the foregoing, it is evident that the process alternative to the one with the lower slope could be oxygen evolution. At higher anodic potentials we have examined the kinetics of oxygen evolution (1, 15) and from these data it is possible to calculate what the rate of oxygen evolution will be in the range of potentials over which the polarization decay occurs at the semicharged electrodes. In Figs. 8*a* and 9*a* are shown the Tafel lines for the anodic oxidation (I) of the semicharged electrode and for oxygen evolution (II) in solutions of the same concentration. The solid lines show the polarization behavior based on i_0 and b values* for each of the alternative processes and the dotted line shows the calculated total rates† over the potential range where I and II have comparable rates. Figs. 8*b* and 9*b* show the same data plotted in terms of the e.m.f. decay lines, the dotted region corresponding to the total rate similarly drawn in Figs. 8*a* and 9*a* and the points the actual e.m.f.'s obtained during an experimental decay run. It is clear from these figures that between 0.1 *M* and 7.3 *M* the inflections in the anodic decay lines are adequately accounted for by the alternative oxygen evolution process which becomes (because of its higher b value) the predominant process at low potentials. We may note that the cathodic lines in Figs. 3*a-d* show no significant inflections; this would be expected since the alternative oxygen process is much slower at the more cathodic potentials. Calculations of the rates of the alternative oxygen evolution process indicate that the inflections in all the anodic decay plots up to 7.3 *M* KOH can be accounted for. However, in the 14.6 *M* KOH solution and in some experiments carried out at 0° C, the oxygen evolution rate is too slow by a factor of about 100 to influence the decay, yet an inflection is observed (Fig. 4*a*) and is also present now in the cathodic line. Furthermore, in the 14.6 *M* solution, the e.m.f. reached at long times is below the reversible oxygen potential so that the oxygen evolution process referred to above cannot be responsible for depressing the e.m.f. to this low value. The electrochemical charging or discharging reaction causes changes of the relative concentrations of water and KOH in the sinter (2, 3, 4) and we show in the Appendix that this effect brings about a concentration polarization in the porous electrode which falls off with time on open-circuit owing to diffusion and gives rise to the inflection in Fig. 4*a*.

(b) Mixed Potentials

From the above, it is seen that the potentials reached at the intersection of the decay lines for solutions up to 7.3 *M* in KOH (or at very long times) must be the mixed potentials corresponding to a finite rate of oxygen evolution and self-discharge on open-circuit. These potentials will be less anodic than the true reversible potentials. From the present data (Figs. 3*a-d*) and our other work (1, 15), we can obtain the polarization parameters

*The method of calculation of these parameters from the decay lines has been discussed previously (11, 1).

†True surface areas of the oxide electrode being unknown, rates in these figures and in Fig. 10 are expressed in amp g^{-1} of Ni(OH)_2 as discussed previously (1).

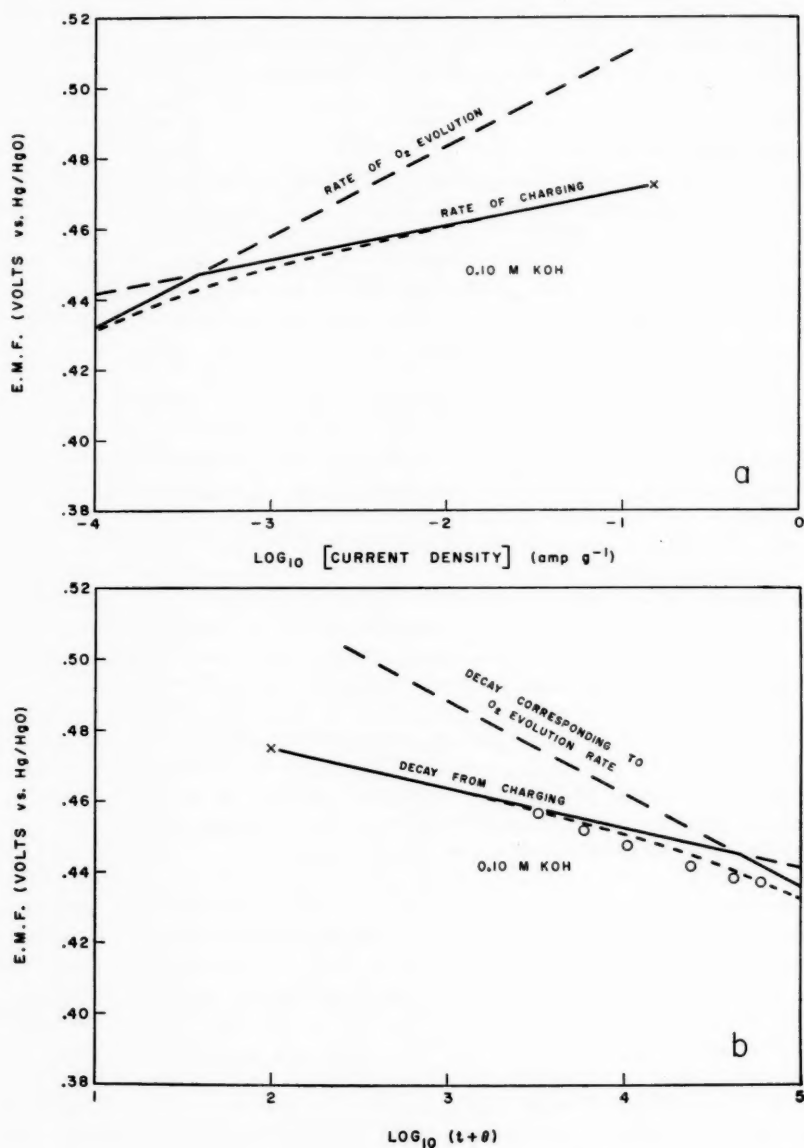


FIG. 8. (a) Tafel lines for anodic oxidation of the semicharged electrode and for O_2 evolution (0.1 M KOH). Line for net current density is broken.

(b) E.m.f. decay lines corresponding to rates of anodic charging and O_2 evolution: dotted line is resultant decay curve; circles, experimental points (0.1 M KOH).

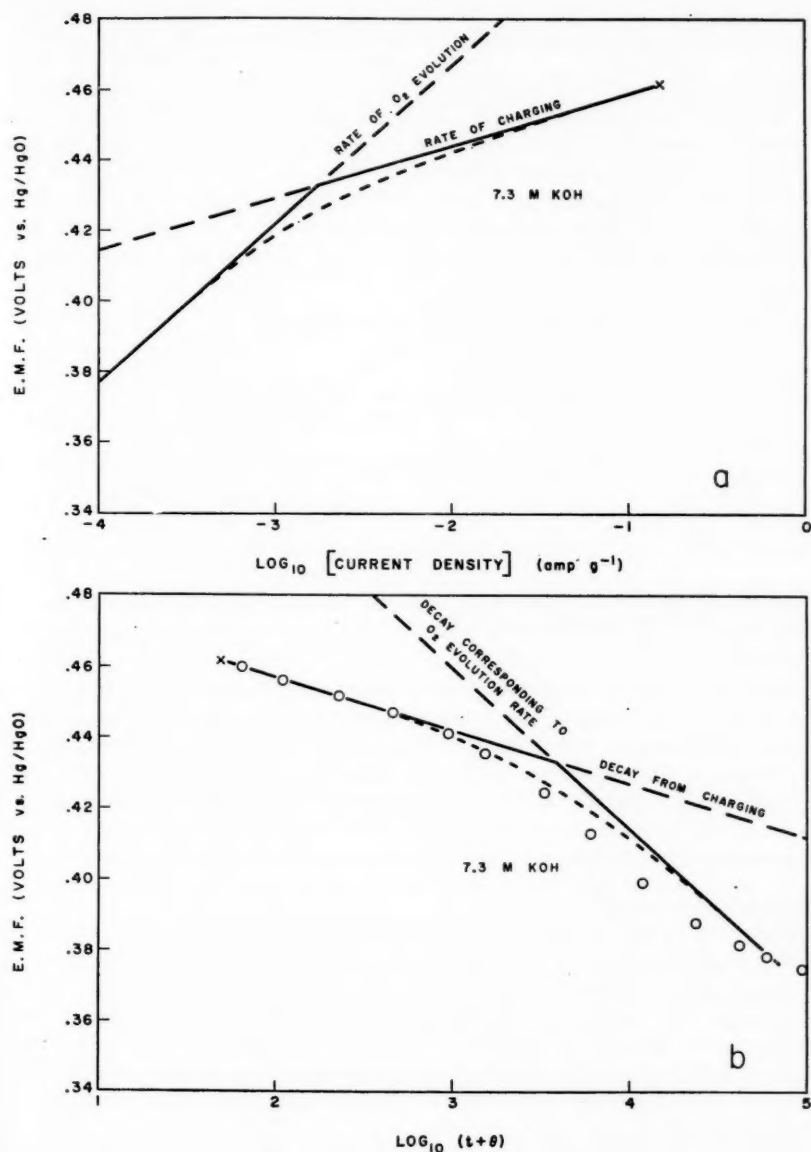


FIG. 9. (a) Tafel lines for anodic oxidation of the semicharged electrode and for O₂ evolution (7.3 M KOH). Line for *net* current density is broken.

(b) E.m.f. decay lines corresponding to rates of anodic charging and O₂ evolution; dotted line is resultant decay curve; circles, experimental points (7.3 M KOH).

i_0 and b for the cathodic and anodic partial "corrosion" reactions, respectively, in the self-discharge process; hence, the mixed potential and the net self-discharge rate at this potential may be calculated as shown in Fig. 10 for 7.3 M KOH solution. In this diagram,

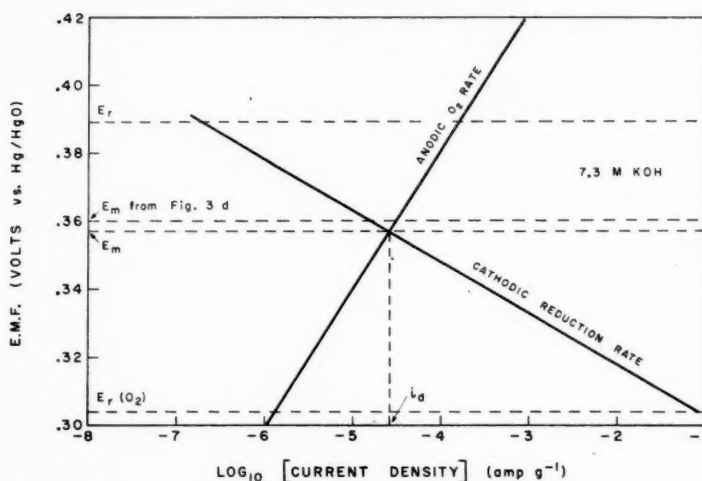


FIG. 10. Polarization lines for the partial reactions in the "corrosion" or self-discharge of the nickel oxide electrode in 7.3 M KOH (symbols are defined in text).

E_m is the steady-state mixed potential, E_r the ideal reversible potential, and i_d the net rate of "corrosion" or self-discharge. It is clear that any e.m.f. measurements (cf. 2, 3, 4) taken on open-circuit at long periods of time, except in the most concentrated solutions and at low temperatures, will not give the true reversible potential E_r but the steady-state mixed potential E_m , which will be lower than E_r by 5–30 mv. Similar figures to 10 may be drawn for the other concentrations of KOH and, except for the 14.6 M KOH solution, the extrapolated or long-time potentials will be E_m .

3. Assignment of Reversible Potentials

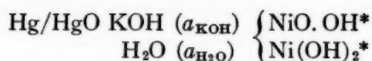
In solutions up to 7.3 M in KOH, the true reversible potentials E_r should be based on extrapolation of the whole region of the cathodic decay lines and that region of the anodic line before which oxygen evolution becomes a significant process, i.e. in the first 3.5 decades of $t+\theta$. The values of E_r thus obtained are shown as circles in Fig. 6 whilst the long-time values or those based on all the decay points (i.e. the E_m values) are indicated by crosses. They differ, as expected, by 5–30 mv. In the derivation of the Nernst equation for the electrode, it is clear that the E_r , and not the E_m values as usually used (2, 3, 4), must be considered.

In the 14.6 M KOH solution, the inflection in the decay line cannot be accounted for at all by the process of oxygen evolution, which is some 100 times too slow in the range of potentials concerned to affect the course of the decay curve. For this solution we can show (see Appendix) that the inflection arises from concentration changes in the electrode which fall off with increasing time after termination of the charging. In this solution and in the saturated KF, the values of potential corresponding to intersection of the cathodic

and anodic decay lines are therefore to be taken as the E_r values, there being no mixed potential in this case.

4. The Nernst Equation for the Electrode

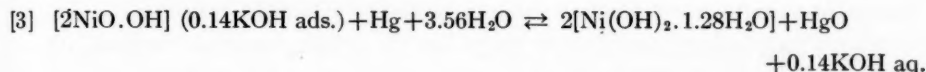
From the above assignment of reversible potentials, we obtain a series of E_r values at various KOH concentrations. Using the data of Akerlöf and Bender (16), these E_r values can be expressed as logarithmic functions of activity of KOH and water. Three unknowns are then involved in the Nernst equation for the potential-determining electrode process viz., E° , and the two coefficients of the logarithmic activity terms. Using the data shown in Fig. 6 for E_r , we may obtain three (or more) simultaneous equations in E_r (experimentally determined), E° , $\ln a_{\text{H}_2\text{O}}$, and $\ln a_{\text{KOH}}$, which give, upon numerical solution, the following Nernst equation at 25° C for the cell



where the * refers to unspecified and probably non-stoichiometric (22, 23, 24) quantities of associated water and adsorbed KOH:

$$[2] \quad E_r = 0.420 (\pm 0.002) - 0.004 (\pm 0.001) \log_{10} [a_{\text{KOH}}] + 0.105 (\pm 0.01) \log_{10} [a_{\text{H}_2\text{O}}],$$

which corresponds to the formal reaction



It will be noted that in this equation terms both in KOH and water activity are required to represent the results, i.e. the dependence of E_r on KOH concentration cannot be quantitatively accounted for through the diminution of water activity with increasing KOH concentration. This residual dependence on KOH activity is consistent and in fair agreement with that deduced from previous work (4) and our own (see below) using a KOH/KF mixture. Chemically, adsorption of KOH at the higher oxide is not inconsistent with the general properties of higher oxides, which are usually more acidic than corresponding lower ones.

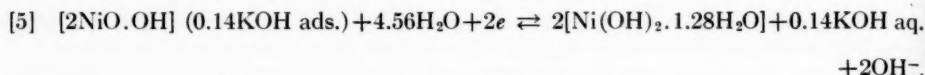
The dependence on water activity is, however, very much greater than that found in Kornfeil's work (4) and is moreover in the *opposite* direction to that found by him. Our results are in qualitative agreement with those of Zedner with regard to direction of the dependence of e.m.f. on water activity. It is unfortunate that Kornfeil's results are presented in an obscure fashion; thus, no *absolute* values of E_r as a function of concentration are stated and the dependence of e.m.f. upon concentration is expressed only as a fraction of the e.m.f. value for a 0.01 M KOH solution, i.e. E° is not stated. Kornfeil's equation

$$[4] \quad E = E^\circ - 0.029 (0.16 \log_{10} a_{\text{H}_2\text{O}} + 0.067 \log a_{\text{KOH}})$$

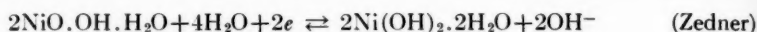
also predicts, using the data of Akerlöf and Bender (16), a minimum e.m.f. at 12 molal KOH, whereas in the present work and in that of Zedner (3) the e.m.f. continues to decrease rapidly with increasing concentration at high concentrations of KOH. Since we have no knowledge of the actual e.m.f. values in Kornfeil's work, it is difficult to seek an explanation of his anomalous results. It may be remarked, however, that the procedure used in his work was different to that used here and involved analytical determinations of the change of KOH and water concentrations relative to that of a KCl or KBr reference

electrolyte. The interpretation of results obtained by this method may be complicated by variation of adsorption of KCl on the electrode with changing KOH concentration and electrode potential. Thus it is well known that Cl^- ions are specifically adsorbed at electrodes particularly at potentials anodic to the potential of zero charge (25).

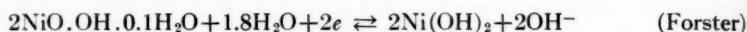
For the single electrode process at the nickel oxide electrode, equation [3] gives



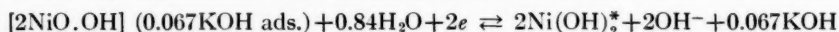
Equations derived by other workers expressed in corresponding form (cf. 4) to that of equation [5] are



and



from which it is seen that apart from the KOH adsorption not considered in the earlier work, our results with regard to dependence on water activity are in closest agreement with those of Zedner. Forster's results (2) differ from the above, possibly on account of the use of nickel oxide electrodes containing graphite. Kornfeil's equation



leads to an anomalously small role of water in the electrode process. Most of the above equations involve non-stoichiometric amounts of hydrate water and this is not inconsistent with available data (22, 23, 24) which indicate non-stoichiometric ranges of hydrate composition.

As an independent check on the validity of our equation [2], the measurements made (Fig. 4b) in saturated KF containing 0.08 *M* KOH enabled a value of E_r to be obtained at a low KOH activity (1.3*), and in which solution the water activity (determined directly by a differential vapor pressure measurement at 25°C) was also low at 0.30. The value of E_r observed experimentally in the KF/KOH mixture was 0.362 v whilst that calculated from equation [2] for the same conditions is 0.364 (6); the agreement is thus within the reproducibility claimed (see Results, Section 3)) in the present work.

Further work, in which the variation of e.m.f. has been studied with degree of oxidation, viz. at states of oxidation greater and less than " $\text{NiO}_{1.25}$ " will be reported elsewhere.

APPENDIX

Diffusion Effects

We show here that the inflection in the anodic decay line for the 14.6 *M* KOH solution can be semiquantitatively accounted for by diffusion effects, which can arise in two ways: (i) from changes of e.m.f. of the electrode itself due to changes of KOH and water activity arising from Faradaic transport and the occurrence of the electrode reaction, and (ii) concentration polarization in the electrode arising secondarily from these concentration changes.

*The activity coefficient for KOH in the mixed electrolyte was taken as that for a solution of pure KOH having the same water activity as that (0.3) in the KF solution. This approximation is justified since at very high ionic strengths, the activity coefficient is determined to a large extent by ion-solvent interaction (19).

During charging, the water and KOH activities near the interface of the electrode material will be higher and lower, respectively, than those in the bulk. After some time, a steady-state activity gradient of water and KOH will be set up in the electrode out towards the solution with a corresponding change in the electrode-solution potential difference. Upon termination of the charging, this activity gradient will fall to zero with attendant e.m.f. changes which will be superimposed on those arising from the "activation controlled" (17) electrode processes discussed above.

It is of interest to make a semiquantitative calculation to establish if these effects could account for the observed inflection in the decay lines in 14.6 *M* KOH.

(a) Model: a finite slab of thickness h is assumed (18) with homogeneous solutions at concentration C_b at the two slab-solution interfaces. (The porous electrode approximates to this since its dimensions were $2.5 \times 1.2 \times 0.1$ cm.) The integrated solution to the diffusion equation for this model is (18)

$$[6] \quad \frac{\bar{C} - C_b}{C_1 - C_b} = \frac{8}{\pi^2} \sum_{\nu=0}^{\infty} \frac{1}{(2\nu+1)^2} \exp \left[- \left(\frac{(2\nu+1)\pi}{h} \right)^2 D t \right]$$

where \bar{C} is the mean concentration of diffusing substance (diffusion constant D) at time t , C_1 the initial concentration (or in the present case, the mean steady state concentration of KOH during charging, prior to decay), and ν the order of the terms required in the Fourier solution of the diffusion equation.

(b) Calculation of concentration changes with time: we cannot make a rigorous calculation of concentration changes with time owing to the complexity of the diffusion problem in a real electrode. However, the following method involving two successive approximations will enable an estimate of the magnitude of the changes of concentration with time to be calculated. Diffusion will occur as soon as any changes of concentration are brought about by the electrolytic charging. At the end of this process, the average concentration in the sinter will hence be less than that which would have arisen had there been no diffusion *during* charging.

As a first approximation, we assume hypothetically that the latter condition obtains and that this results in a change of mean concentration $\Delta\bar{C}$. The fall of $\Delta\bar{C}$ (with no current passing) with time is then calculated from equation [6] and from this plot rates of change of mean concentration $d\bar{C}/dt$ can be calculated at various times. As a second approximation, we then obtain that value of $d\bar{C}/dt$ from the values discussed above, which corresponds to the rates of production of water and removal of KOH, respectively, during charging. This value of $d\bar{C}/dt$ will then be relevant to that time at which the current is interrupted for decay measurements. In the first approximation treatment, this rate of change of concentration would have been reached after a time t' . The subsequent decay of $\Delta\bar{C}$ with time t after the *actual* termination of charging is then calculated and plotted against t and this concentration change $\Delta\bar{C}$ after the times t would be equivalent to the same changes of concentration after times $t+t'$ in the first approximation calculation. This procedure will thereby allow approximately for the fact that during electrolysis some steady state change of concentration will tend to have been set up which will be less than that occurring if no diffusion took place. Two alternative values of D in equation [6] were taken as 10^{-6} and 3×10^{-7} cm² sec⁻¹ in order to place limits on the resulting e.m.f. variation which could arise from uncertainties in the value of D . The above values were estimated from data at low concentration (19) by correction for the relative viscosity (η_r) of 14.6 *M* KOH ($\eta_r = 12$) and after empirical allowance

for the fact that, in the porous electrode, the diffusion path length will probably be somewhat longer than that corresponding to the free linear diffusion and the fact that the channel area available for diffusion out of the electrode will be less than the projected area of the electrode. The values of D taken are probably of the right order of magnitude but cannot be regarded as more precise than this.

From the changes of concentration calculated by the above procedure, the total change of e.m.f., ΔE_e , with time, due to diffusion effects, can be calculated using equations [2] and the data given by Akerlöf and Bender (16) for concentration cells in KOH and water.

The calculated values of ΔE_e are shown for 14.6 M KOH in Fig. 4a as a function of time during decay and is seen that ΔE_e is comparable with the total anodic polarization observed and can hence account fairly well for the form of the inflected decay line in 14.6 M KOH. Similar considerations apply to the cathodic line where effects in an opposite direction will occur. It may be noted that no value of θ exists which can lead to linearity of the decay curve in Figs. 4a or 4b.

We can therefore conclude that the potential to be taken as the reversible one in 14.6 M KOH (Fig. 4a) is that corresponding to the intersection of the anodic and cathodic decay lines after the longest times. The same conclusions will apply to the results in saturated KF solution (Fig. 4b).

Diffusion effects will be much less significant in the more dilute and less viscous solutions since it may readily be shown that ΔE_e values are much smaller and the times over which diffusion equilibration is occurring are much shorter (owing to the higher diffusion constants) than those for the 14.6 M solutions. For the more dilute solutions, the inflections arise, as discussed above, from the alternative oxygen evolution process.

It can be shown that these effects in dilute solution are operative over periods of time comparable to θ (the time correction applied to allow for a finite charging rate). Thus diffusion effects are absorbed in the empirical assignment of θ . This will introduce some uncertainty in its value but will have no significant effect on the slope of the anodic and cathodic decay lines since θ in these cases is not larger than about 100 seconds.

ACKNOWLEDGMENTS

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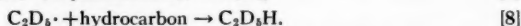
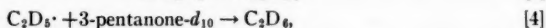
HYDROGEN ATOM ABSTRACTION BY ETHYL- d_5 RADICALS. PART I¹

P. J. BODDY² AND E. W. R. STEACIE

ABSTRACT

The photolysis of 3-pentanone- d_{10} has been used as a source of deuterated ethyl radicals and some of their hydrogen abstraction reactions studied over the temperature range 50–300° C.

The compounds neopentane, *n*-butane, and isobutane were chosen as representative of the basic structural features in the alkane series. The activation energies for abstraction ($E_s - \frac{1}{2}E_2$) are respectively 12.60 ± 0.7 , 10.4 ± 0.75 , and 8.9 ± 0.6 kcal/mole and the pre-exponential factors ($\log_{10}(A_s/A_4)$) are 0.300 ± 0.09 , 0.082 ± 0.09 , and -0.334 ± 0.066 where



For abstraction of a deuterium atom from the ketone the values obtained are $E_4 - \frac{1}{2}E_2 = 9.0 \pm 0.5$ kcal/mole and ($\log_{10}(A_4/A_2^{\frac{1}{2}})$) = 8.36 ± 0.20 in agreement with previous investigations (1, 2).

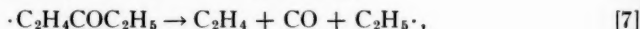
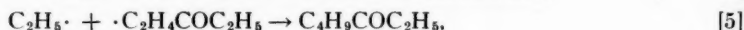
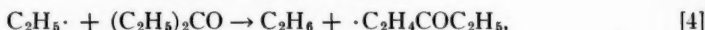
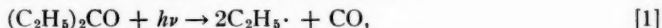
The value of the disproportionation to combination ratio for C_2D_5 radicals is 0.0985 ± 0.008 independent of temperature.

INTRODUCTION

Although a great deal of information has been obtained on the abstraction of hydrogen atoms from hydrocarbons by methyl radicals, there is little information on more complex alkyl radicals. The methyl radical work has led to the realization of a relationship between structural features of hydrocarbon molecule reactants and activation energy for abstraction of a hydrogen atom (3). This, however, has not in turn led to any good theoretical treatment of the problem probably, at least in part, because there is so little experimental data on the influence of the structure of the alkyl radical itself. There is published data on the abstraction by ethyl radicals from some unsaturated hydrocarbons in the C_6 and C_8 range (4) and this does throw light on the effect of bond multiplicity but not on the aspects of alkane structure.

The major difficulty with higher radicals is that of analysis of the reaction products. In the case of ethyl radicals, calculation of the rate constant for abstraction involves determination of small quantities of ethane, ethylene, and *n*-butane. This severely complicates investigation of some of the most interesting hydrocarbons.

The mechanism of 3-pentanone photolysis is known to be (5)



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²N.R.C. Postdoctorate Fellow 1957–59. Present address: Bell Telephone Laboratories, Murray Hill, New Jersey, U.S.A.

Under suitable conditions the ethane from [3], and [4] can be assessed and hence the rate of [8] determined.

The situation can be greatly simplified by the use of labelled species. The use of deuterated hydrocarbon molecules is possible but does not lead to results directly comparable with the large number of experiments carried out with methyl and perfluoralkyl radicals and hydrogenated molecules without making certain assumptions about the relative reactivities of C—H and C—D bonds. A study has been made of the reaction between ethyl radicals and deuterium molecules (6) and from this the activation energy for abstraction from a hydrogen molecule deduced. The value obtained agrees reasonably well with that determined experimentally for ethyl- d_5 radicals and hydrogen (7).

A preferable experiment involves the use of a deuterated radical source with hydrogenated molecules. Current evidence suggests that insofar as activation energy for hydrogen atom abstraction is concerned, deuterated radicals behave identically with their hydrogenated counterparts within the present limits of experimental error (4, 8, 9). Analysis of products is greatly simplified since only reactions [4] and [8] need to be considered and from the ratio of (in this case) C_2D_5H/C_2D_6 the activation energy difference between [4] and [8] may be determined. (C_2D_6 from [3] is easily estimated.)

The reasonable assumption is made here that the mechanism outlined above for 3-pentanone- d_0 is entirely applicable to the photolysis and subsequent reactions of 3-pentanone- d_{10} , although the rate constants for the individual steps will, of course, be different.

EXPERIMENTAL

A conventional high vacuum apparatus was used with sections for storage, purification, reaction, analysis, and sampling of gases as previously described in papers from this laboratory. Mercury cutoffs were used at all points where absorption of organic vapors could lead to error.

The reaction system was a 10-cm-long quartz cell with an all glass circulating pump in the connecting tubing, the total volume being 196 ml. Both the cell and the metal valves isolating it from the rest of apparatus were contained in an air thermostat. The cell itself was surrounded by a cylindrical electric furnace which was maintained to within 1° C of the required temperature. Pressures were measured on a quartz spiral gauge within the thermostat.

Radiation from a Hanovia S-500 lamp was collimated by an aluminum cylinder and then brought to a parallel beam, which just filled the cell, with a quartz lens. A 2-mm-thick "Pyrex" filter removed radiation below 2900 Å.

The reaction products were distilled several times at -80° C to remove most of the unphotolysed ketone and involatile products, and then passed through traps at -165° C, -125° C, and -215° C in that order. Carbon monoxide passed straight through. C_2 hydrocarbons were collected at -215° C. The fraction between -125° C and -165° C was n -butane- d_{10} (this was measured only in experiments where the ketone was photolysed alone).

MATERIALS

3-Pentanone- d_{10} was obtained from Merck of Canada. It was degassed and stored in a blackened bulb behind a mercury cutoff. Small samples were further degassed before each run. The purity of the ketone is discussed below.

Neopentane, *n*-butane, and isobutane were all Phillips Research Grade materials. They were degassed and stored in the same way as the ketone. Their purities exceeded 98%.

TREATMENT OF DATA

1. Ketone

The low energy (15 v) mass spectrum of the ketone, showing only parent peaks, gave the following analysis, assuming equal sensitivities:

- (1) $C_4D_{10}CO$ 93.7%,
- (2) C_4D_9HCO 5.95%,
- (3) $C_4D_8H_2CO$ 0.34%.

The peaks were small due to the low sensitivities at 15 v and the smallest peak was difficult to measure.

The normal (70 v) spectrum gave information on the relative abundance of species 1 and 2.

Parent peaks	95 pk/96 pk = 5.25%.
Propionyl peaks	61 pk/62 pk = 2.8% (\equiv 5.6% of species 2).
Ethyl peaks	33 pk/34 pk = 2.5% (\equiv 5.0% of species 2).

The latter two ratios include the effect of species 3 but since the values lie on either side of the direct ratio of the parent peak the effect of this appears to be well within the experimental error. An average value of 5.3% of species 2 was adopted. In view of the relative abundances of species 2 and 3 it was assumed that 3 was largely $(C_2D_4H)_2CO$ (since 0.0595² is very close to 0.0034, the value obtained at low energy). In previous work with this ketone, prepared by the same method (heavy water exchange with $(CD_3CH_2)_2CO$), it was logically assumed that the H atoms were mainly in the primary position (1). A similar assumption is made here.

The composition of the ketone used in the following experiments was therefore taken to be:

- (1) $(C_2D_5)_2CO$ 94.4%,
- (2) $CD_2HCD_2COC_2D_5$ 5.3%,
- (3) $(CD_2HCD_2)_2CO$ 0.28%.

The relative abundance of 3 has been adjusted to .053².

2. Butanes

The butane produced in reaction [2] should have an isotopic composition similar to that of the original ketone. Only the 70 v spectrum was taken so no butane with two H atoms could be detected with accuracy. The ratio C_4D_9H/C_4D_{10} was in good agreement with the expected value of 0.053 over the whole range of experimental conditions. C_4D_{10} was taken as 94.4% of total butane in most runs, but the ratio was checked at intervals and found to be constant. The uncertainty introduced by not analyzing the $C_4D_8H_2$ was negligible.

3. C_2 Hydrocarbons

(a) Ethanes

C_2D_6 can arise in three ways:

- (i) $C_2D_5\cdot + \text{ketone} \rightarrow C_2D_6$, which we wish to determine.

(ii) $C_2D_5\cdot + C_2D_5\cdot \rightarrow C_2D_6 + C_2D_4$; this can be estimated from the C_2D_4 after correction has been made for other sources.

(iii) $C_2D_5\cdot + C_2D_4H\cdot \rightarrow C_2D_6 + C_2D_3H$; this can be estimated from the C_2D_3H yield.

C_2D_5H can arise from:

(iv) $C_2D_5\cdot + \text{hydrocarbon} \rightarrow C_2D_5H$, which we wish to determine.

(v) $C_2D_5\cdot + \text{ketone} \rightarrow C_2D_5H$; an empirical correction curve for this is described later.

(vi) $C_2D_4H\cdot + \text{ketone} \rightarrow C_2D_5H$ assuming the ketone composition given above and assuming that there is no different rate of photolysis, or reaction of the two types of radical about 3.0% should be $C_2D_4H\cdot$. Hence C_2D_5H from (vi) should be 3.0% of C_2D_6 from (i).

Preliminary results showed that the ratio of disproportionation to combination for ethyl- d_5 was about 0.1 compared with 0.14 for ethyl- d_0 radicals (5). The activation energy for these reactions is very close to zero, and the collision numbers cancel from each ratio. Assuming that the steric factors for combination in the two cases are equal since the radicals are so similar, then on a collision-for-collision basis C—H bonds break 1.4 times more frequently than C—D bonds in the disproportionation reaction. If these relative rates hold good for abstraction from $CD_2HCD_2\cdot$ and bearing in mind the head-to-tail mechanism of disproportionation (2, 15), the relative rates of abstraction of D and H stand in the ratio 2:1.4. Since $C_2D_4H\cdot$ represents about 3.0% of the total radical concentration then reaction (iii) above should represent $((2/3.4) \times 3.0\%) = 1.75\%$ of the total disproportionation reaction. Since C_2D_4 is produced in all disproportionation reactions except (iii) and in negligible amounts in other ways below 197°C, the C_2D_4 yield can be taken to represent the total disproportionation. Figure 1, in which C_2D_3H/C_2D_4 from a series of experiments with the ketone alone is plotted vs. temperature, shows that in the range 50–150°C the ratio comes close to that predicted. At 180°C and above

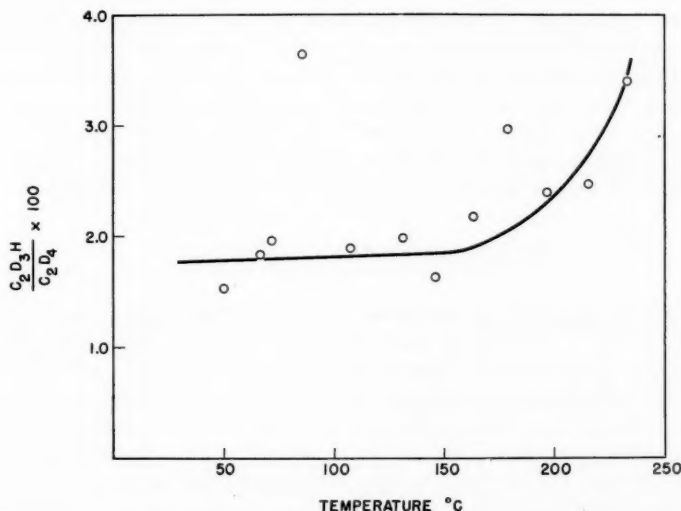


FIG. 1. Ratio of C_2D_3H to C_2D_4 in $DEK-d_{10}$ photolysis.

the ratio increases, probably due to decomposition of pentanonyl radicals, which would be hydrogen enriched if the hydrogen is primary. If there is no isotope effect on the decomposition, about 3% of the ethylene from this source would be C_2D_3H .

(vii) $C_2D_5\cdot + CD_2HCD_2\cdot \rightarrow C_2D_5H + C_2D_4$; on the basis of the above discussion this should be $((1.4/3.4) \times 3.0\% =) 1.25\%$ of the total disproportionation reaction.

(viii) $CD_2HCH_2\cdot + C_2D_5 \rightarrow C_2D_5H + C_2D_4$, 3.0% of the total disproportionation.

Since the $C_2D_4H\cdot$ concentration is relatively low, interactions between these radicals and with impure ketone are not considered.

(b) *Ethylenes*

C_2D_4 can arise in four ways:

(ii) $C_2D_5\cdot + C_2D_5\cdot \rightarrow C_2D_6 + C_2D_4$, the major source when (ix) is not significant.

(vii) $C_2D_5\cdot + C_2D_4H\cdot \rightarrow C_2D_5H + C_2D_4$, 1.25% of the total disproportionation.

(viii) $C_2D_4H\cdot + C_2D_5\cdot \rightarrow C_2D_5H + C_2D_4$, 3.00% of the total disproportionation.

(ix) $C_2D_4COC_2D_5 \rightarrow C_2D_4 + CO + C_2D_5\cdot$; this reaction is of little importance below 200° C. Under these circumstances 4.25% of the C_2D_4 arises from (vii) and (viii), the remainder from (ii).

C_2D_3H can arise only in (iii) and is discussed above.

On the basis of these corrections the data was treated in the following way. The measured $R_{C_2D_6}$ was converted to that produced in (i) by subtracting the $R_{C_2D_4}$ from (ii) (i.e. 95.75% of the total $R_{C_2D_4}$) and $R_{C_2D_3H}$. $R_{C_2D_5H}$ was corrected by subtracting 3.0% $R_{C_2D_6}$ (vi) and 4.25% of the total $R_{C_2D_6}$ (vii) and (viii).

When this procedure had been carried out for the experiments in which the ketone was photolysed alone there was a small residue of C_2D_3H . This could have been largely removed by adjustment of the correction factors but it was preferred to treat it as a separate temperature-dependent correction due to reaction (v). The function $(R_{C_2D_3H} \text{ residual}) / (R_{C_4D_{10}}^{\dagger}[\text{ketone}])$ is plotted vs. $1/T$ in Fig. 2, which was used as a correction curve for subsequent experiments. The results are not sufficiently precise to ascribe an activation energy and hence check the position of the H atom in the ketone molecule.

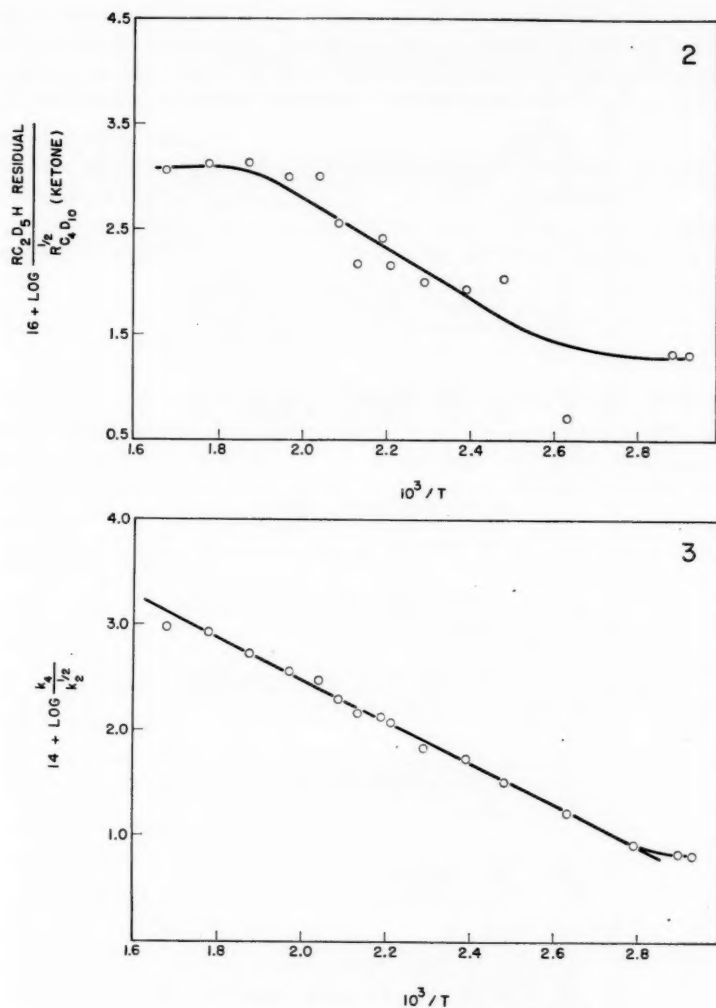
While the corrections are complex, they are generally not large and the final results are not greatly affected by the approximate nature of some of the corrections.

RESULTS

Ketone Photolysis

The data obtained for photolysis of the ketone alone are presented in Table I. Columns 10, 11, and 12 have been corrected as described. In the region where reaction [7] is negligible column 12 represents k_3/k_2 . Below 197° C the values are in good agreement (0.0985 ± 0.008) and independent of temperature. At higher temperatures this value of k_3/k_2 is used to calculate $R_{C_2D_6}$ from [2] by measurement of $R_{C_4D_{10}}$ from [3]. The corrections described in the previous section are valid only when $R_{C_2D_4}$ from [7] is negligible. Experiments were carried out up to a temperature where the activation energy plot showed a curvature (300° C) indicating the onset of a systematic error in the correction.

It can easily be shown that in the valid range $(k_4/k_2^{\dagger}) = R_{C_2D_6} \text{ corrected} / R_{C_4D_{10}}^{\dagger}[\text{ketone}]$.

FIG. 2. Correction curve for residual C_2D_5H .FIG. 3. Activation energy plot for $C_2D_5 + \text{DEK}-d_{10}$.

The data are plotted vs. $1/T$ in Fig. 3. The results calculated by the least squares method are compared with previous values below:

	<i>C</i>	<i>B</i>	$13 + \log_{10} A_4/A_2^{1/2}$	$E_4 - \frac{1}{2}E_2$
(a) Wijnen and Steacie	5.455	2.008	5.5 ± 0.2	9.2 ± 0.4
(b) James and Steacie	5.750	2.113	5.7 ± 0.2	9.6 ± 0.4
(c) Boddy and Steacie	5.360	1.948	5.4 ± 0.2	9.0 ± 0.5

In (a) 2,2',4,4'-tetradeuterodiethyl ketone was used and the data refers to abstraction of α -D. In (b) and (c) the data refers to the over-all abstraction involving both α - and β -D.

TABLE I

Ketone, mol./ml $\times 10^{-17}$	Temp., °K	Time, sec	$R_{C_2D_6}$	$R_{C_2D_3H}$	$R_{C_2D_4}$	$R_{C_2D_3H}$ $\times 10^{-12}$ in mol./ml sec	$R_{C_4D_{10}}$	R_{CO}	$R_{C_2D_3H}$ res	$R_{C_2D_6}$ corr	$R_{C_2D_3H}$ res	$\log \frac{R_{C_2D_3H} \text{ res}}{R_{C_4D_{10}}}$	$\log \frac{k_1}{k_2}$
5.70	452	3600	1.28 ₂	0.0548	0.260	0.0077	2.32 ₆	—	1.026	0.1067	0.0128	2.1673	2.0712
7.34	437	3600	1.02	0.0456	0.272	0.0059	2.44 ₇	3.74 ₇	0.754	0.1062	0.0113	1.9924	1.8169
2.96	404	4410	0.295	0.0155	0.172	0.0034	1.77 ₃	3.04 ₆	0.127 ₈	0.0926	0.0043	2.0382	1.5091
6.00	380.5	3720	0.454	0.0182	0.296	0.0056	2.89 ₁	4.09 ₇	0.165 ₇	0.0977	0.0053	0.7153	1.2103
7.04	359	3960	0.474 ₆	0.0128	0.367	0.0134	3.45 ₄	4.93 ₅	0.110 ₇	—	—	—	0.9273
17.26	470	3720	4.86 ₁	0.198 ₆	0.481	0.0115	3.11 ₈	7.98 ₈	4.397 ₇	0.1473	0.0462	2.1798	2.1741
7.38	419	3720	0.731	0.033	0.185	0.0030	1.82 ₁	2.70 ₁	0.551 ₃	0.0964	0.0086	1.9345	1.7423
12.60	339	3723	0.326 ₃	0.0166	0.210	0.0038	2.10 ₄	2.60	0.122	0.0939	0.0039	1.3308	0.8240
12.60	344.5	3600	0.338	0.0172	0.217	0.0040	2.10 ₄	2.55 ₂	0.126 ₈	0.0984	0.0041	1.3489	0.8414
8.59	489	3300	2.33 ₈	0.142 ₉	0.119 ₉	0.0029	0.729	—	2.22 ₁	0.1565	0.074	3.0000	2.4893
8.81	507.5	3600	2.51 ₈	0.143 ₁	0.0705	0.0024	0.575	2.55 ₂	2.44 ₉	0.1170	0.067	2.9560	2.5655
11.40	323	4780	0.231 ₆	0.013 ₆	0.177 ₇	0.0027	1.84 ₅	—	0.0592	0.0919	0.0041	1.4220	0.5834
8.68	534	2915	3.11	0.171	0.048 ₈	0.0025	0.441	—	3.04 ₂	0.1045	0.078	3.1290	2.7218
8.23	563	4191	3.30 ₄	0.150	0.181	0.031	0.218	—	3.250	0.795	0.0515	3.1270	2.9273
10.17	456	3600	1.61 ₆	0.0775	0.109	0.0158	1.16	—	1.48 ₆	0.0940	0.0278	2.4090	2.1373
10.38	479	3600	1.93 ₆	0.0918	0.0905	0.0159	0.805	—	1.84 ₁	0.1075	0.033	2.5495	2.2961
10.68	597	3600	5.50	0.228	0.0921	0.0917	0.262	—	5.38	3.370	0.0654	3.0630	2.9928

The constants are those in the expression $13 + \log_{10}(k_4/k_2^{1/2}) = C - (B.10^3/T)$.

The present results confirm the conclusion that there is negligible effect of isotopic substitution on the reactivity of ethyl radicals. It was important to redetermine the ketone data here since subsequent activation energies were measured relative to this.

Ketone and Hydrocarbons

The data from the experiments with neopentane, *n*-butane, and isobutane appear in Tables II, III, and IV.

Activation energies may be obtained in two ways. The most precise way is to consider the reactions [4] and [8]. The activation energy difference $E_8 - E_4$ may be obtained by plotting

$$\log_{10} \frac{R_{C_2D_5H} \text{ corrected}}{R_{C_2D_6} \text{ corrected}} \cdot \frac{[\text{ketone}]}{[\text{hydrocarbon}]} \text{ vs. } \frac{1}{T} \quad (\text{Fig. 4}).$$

The isobutane curve falls off below 110° C. This was due to the use of too low an isobutane to ketone ratio and hence to too low a $R_{C_2D_5H}$ to $R_{C_2D_6}$ ratio leading through small errors in the correction factors to a large systematic error in $R_{C_2D_5H} \text{ corrected}$. Increase of the relative isobutane pressure gave the point close to the drawn line ($1/T = 2.64$).

Least squares calculation gives:

For neopentane

$$E_{8a} - E_4 = 3.6 \pm 0.2 \text{ kcal},$$

$$\log_{10}(A_{8a}/A_4) = 0.30 \pm 0.09;$$

hence $E_{8a} - \frac{1}{2}E_2 = 12.6 \pm 0.7 \text{ kcal},$

$$(A_{8a}/A_4) = 2.00 \pm 0.5.$$

For *n*-butane

$$E_{8b} - E_4 = 1.38 \pm 0.25 \text{ kcal},$$

$$\log_{10}(A_{8b}/A_4) = 0.082 \pm 0.09;$$

hence $E_{8b} - \frac{1}{2}E_2 = 10.4 \pm 0.75 \text{ kcal},$

$$(A_{8b}/A_4) = 1.21 \pm 0.27.$$

For isobutane

$$E_{8c} - E_4 = 0.1 \pm 0.1 \text{ kcal},$$

$$\log_{10}(A_{8c}/A_4) = 1.666 \pm 0.066;$$

hence $E_{8c} - \frac{1}{2}E_2 = 8.9 \pm 0.6 \text{ kcal},$

$$(A_{8c}/A_4) = 0.464 \pm 0.07.$$

Alternatively, $R_{C_2D_4}$ may be used to calculate $R_{C_4D_{10}}$ from k_3/k_2 and then by plotting $\log_{10}(R_{C_2D_5H} \text{ corrected}/R_{C_4D_{10}}^{1/2} [\text{hydrocarbon}])$ vs. $1/T$, $E_8 - \frac{1}{2}E_2$ may be obtained directly. This method suffers from the very unfavorable value of k_3/k_2 which multiplies errors in $R_{C_2D_4}$ in the final expression. This limits the range of validity of the experiments since it is so sensitive to $R_{C_2D_4}$ from [7] and also increases the scatter over the range where the analysis is valid. The results plotted in Fig. 5 are, however, compatible with those from the first method.

The data for abstraction from the ketone in the presence of hydrocarbons is plotted in Fig. 6. The line is drawn to correspond to that in Fig. 3. In view of the greater complexity of these systems the agreement is considered satisfactory.

TABLE II

Ketone, mol./ml $\times 10^{-17}$	Neopentane, mol./ml $\times 10^{-17}$	Temp., ° K	Time, sec	$R_{C_2D_6}$	$R_{C_2D_4}$	$R_{C_2D_3H}$	$R_{C_2D_3H}$ corr	$R_{C_2D_6}$ corr	2+ $\log \frac{k_{40}}{k_4}$	13+ $\log \frac{k_4}{k_2^3}$	15+ $\log \frac{k_{40}}{k_2^3}$
5.26	11.9	556	4830	1.42 ₆	0.125	—	1.12 ₁	6.49	0.8837	—	—
5.79	13.0	525	4000	1.08 ₁	0.291	0.0313	0.756 ₆	5.60 ₁	0.7800	—	—
5.86 ₅	9.19	494	4565	4.06 ₅	0.34 ₆	0.007	0.283 ₅	0.6860	0.6860	—	—
6.22	12.3 ₅	473	4250	0.379	0.508	0.0977	0.230	2.64	0.6425	—	—
5.61	18.8	452.5	4317	0.277	0.496 ₇	0.0182	0.187	1.44 ₁	0.5900	1.0590	1.6470
5.99	18.2	435	3935	0.173 ₆	0.497	0.0147	0.105 ₅	1.02 ₁	0.5300	0.8810	1.4116
8.35	66.7	358.5	3620	0.0295 ₅	0.258	0.00276	0.152	0.152	0.1106	0.1240	0.2330
9.09	51.5	377	3600	0.089	0.331 ₇	0.0103	0.0236	0.237	0.2455	0.4400	0.6850
7.78	65.4 ₅	422	4440	0.144	0.544	—	0.119 ₄	0.496	0.4580	0.9500	1.4065
5.24	32.5 ₅	575	3160	0.943	0.0503	—	0.687	1.61 ₃	0.9731	—	—
6.07	37.1	597	3600	1.33 ₄	0.491	0.034	1.25	1.97 ₂	1.0157	—	—

TABLE III

Ketone, mol./ml $\times 10^{-17}$	n-Butane, mol./ml $\times 10^{-17}$	Temp., ° K	Time, sec	$R_{C_2D_6}$	$R_{C_2D_4}$	$R_{C_2D_3H}$	$R_{C_2D_3H}$ corr	$R_{C_2D_6}$ corr	1+ $\log \frac{k_{40}}{k_4}$	13+ $\log \frac{k_4}{k_2^3}$	13+ $\log \frac{k_{40}}{k_2^3}$
3.86	3.27	525.5	4000	1.30	0.0781	0.0239	1.11 ₃	3.91 ₉	0.5250	—	—
4.86	3.56	505	3700	1.07 ₁	0.195	0.0104	0.832 ₂	3.79 ₄	0.4757	—	—
4.73 ₅	2.85	467	3700	0.402 ₆	0.338	0.0152 ₄	0.307 ₈	1.83 ₂	0.4456	1.3198	1.7657
5.18	4.51	445.5	3600	0.414	0.441	0.0127	0.319 ₅	1.44 ₄	0.4074	1.0319	1.4370
5.08 ₅	4.46	406	7280	0.150	0.506	0.0195	0.102 ₅	0.633 ₈	0.3152	0.6912	1.0043
4.95	5.88	394	3600	0.125	0.566	0.0237	0.084	0.334 ₃	0.3243	0.2967	0.7747
2.60	60.5	379	3600	0.234 ₉	0.0643	—	0.230 ₁	0.0465	0.3269	0.3439	0.6721
9.13	43.5 ₅	412.5	3620	0.319 ₂	0.00561	—	0.303 ₆	0.292 ₇	0.3373	0.6286	0.9659
7.12	47.6	529	3600	2.04 ₇	—	—	2.00 ₅	0.4900	0.4900	—	—
7.83	42.2	543	3600	2.55 ₅	—	—	2.49 ₄	1.37 ₂	0.5272	—	—
3.64	41.9	575	3600	3.670	—	—	3.63 ₄	0.898 ₇	0.5463	—	—
5.41	37.6	598	4310	4.86 ₄	0.887	0.597	4.80 ₄	1.71 ₈	0.6104	—	—

TABLE IV

Ketone, mol./ml $\times 10^{-17}$	Isobutane, mol./ml $\times 10^{-17}$	Temp., ° K	Time, sec	$R_{C_2D_5H}$	$R_{C_2D_5}$	$R_{C_2D_4}$ $\times 10^{-12}$ in mol./ml sec	$R_{C_2D_3H}$	$R_{C_2D_3H}$ corr	$R_{C_2D_3H}$ corr	$1 + \log \frac{k_{ac}}{k_4}$	$13 + \log \frac{k_4}{k_2}$	$13 + \log \frac{k_{ac}}{k_2}$
12.0 ₈	3.64 ₆	522	3610	2.54	12.8 ₉	0.0403	0.0326	12.8 ₂	1.90 ₁	0.6925	—	—
10.4 ₉	2.77	488	3725	0.974	5.72	0.598	0.0307 ₅	5.12	0.675 ₆	0.6989	—	—
15.7 ₇	2.58	456.5	3600	0.959	8.21	0.858	0.0575	7.23	0.601	0.7056	1.1900	1.8960
10.4 ₃	2.63	440	3600	0.565	4.01	0.781	0.032	3.23	0.392 ₅	0.6822	1.0422	1.7251
15.3 ₆	3.75	424.5	4630	0.587	4.15	0.973	0.0443	3.17 ₄	0.404	0.7165	0.8182	1.5349
11.1 ₄	2.96	408.5	3400	0.329 ₆	2.55 ₈	0.937 ₆	0.035	1.62 ₈	0.219 ₁	0.7065	0.6739	1.3791
6.01	10.7 ₇	562	3600	0.732	0.798	0.0435	—	0.757	0.707 ₈	0.7177	—	—
6.18	19.6 ₄	531	3640	1.41 ₈	0.806	—	—	0.896	1.39 ₁	0.6893	—	—
9.24	31.0 ₆	574	3000	2.45 ₄	1.48 ₄	—	—	1.48 ₄	2.41 ₁	0.6830	—	—
6.48	28.6 ₃	592	3600	2.08 ₂	0.957	—	—	0.957	2.05 ₃	0.6855	—	—
11.9 ₈	3.42	395	3600	0.261	2.37 ₇	1.05 ₄	0.0369	1.33	0.158	0.6191	0.5308	1.1501
11.8 ₃	3.78	375.5	3675	0.157	1.65 ₄	0.965	0.0365	0.697	0.082	0.5658	0.2747	0.8407
10.1 ₅	3.62	360	4400	0.092	1.21	0.861	0.0448	0.353	0.0385	0.4810	0.0682	0.5551
8.10	56.5 ₄	378	4370	1.07 ₄	0.445	0.192	—	0.261 ₆	1.05 ₅	0.7612	0.3636	1.1255

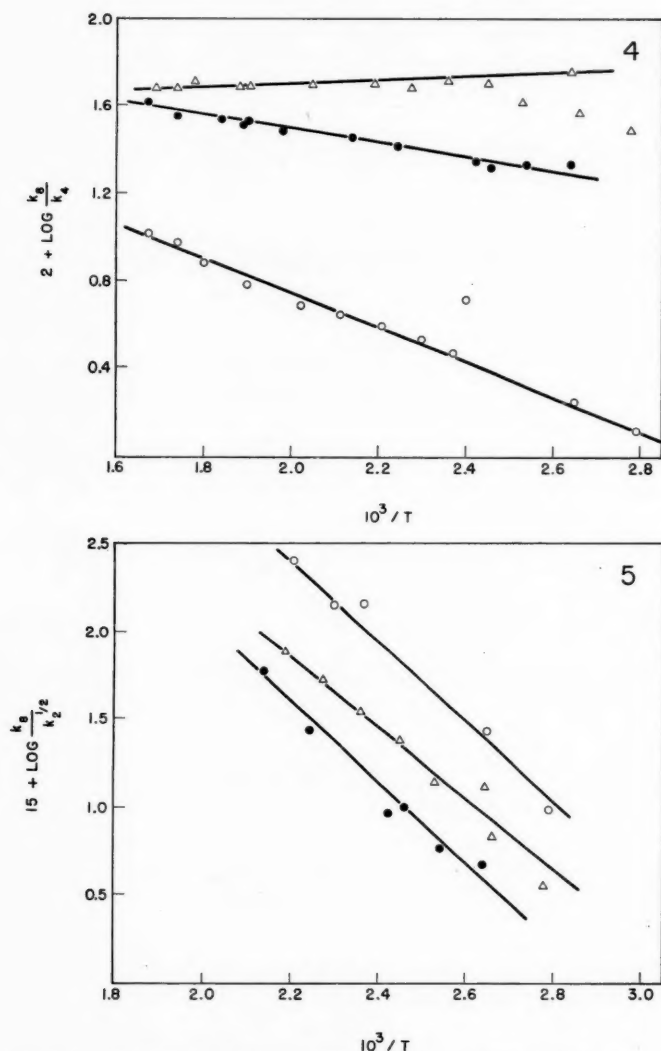


FIG. 4. Activation energy difference between $C_2D_5 + \text{hydrocarbon} \rightarrow C_2D_5H$ and $C_2D_5 + DEK \cdot d_{10} \rightarrow C_2D_6$.
 FIG. 5. Activation energy plot for $C_2D_5 + \text{hydrocarbons}$.

DISCUSSION

The results obtained for ethyl- d_5 radicals are compared below with those corresponding for methyl (9). In both cases the results are approximately corrected for the presence of primary hydrogen atoms in the two butanes by using the rate per primary hydrogen atom from the neopentane experiments. The behavior in the two cases is parallel in that there is a change in reactivity of about an order of magnitude as one goes from primary to secondary to tertiary hydrogen atoms.

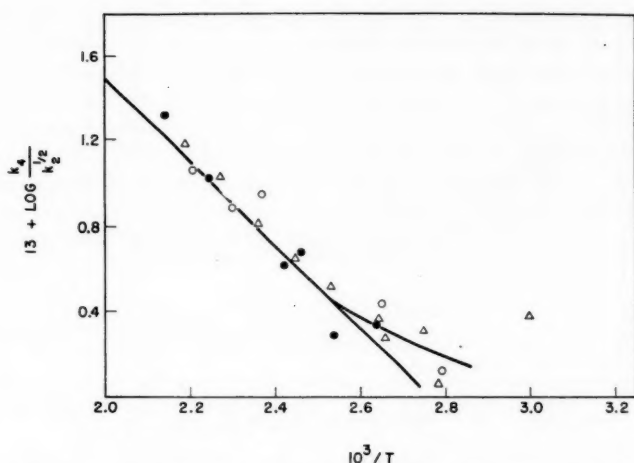
FIG. 6. Activation energy plot for $C_2D_5 + DEK \cdot d_{10}$ in the presence of hydrocarbons.

TABLE V

	$C_2D_5 \cdot$			$CH_3 \cdot$		
	$E_0 - \frac{1}{2}E_2$ in kcal	$k_0/k_2^{\frac{1}{2}} \times 10^{13}$ at 182° C	$k_0/k_2^{\frac{1}{2}} \times 10^{13}$ per "active" H atom	$E_1 - \frac{1}{2}E_2$ in kcal	$k_1/k_2^{\frac{1}{2}} \times 10^{13}$ at 182° C	$k_1/k_2^{\frac{1}{2}} \times 10^{13}$ per "active" H atom
neo- C_5H_{12}	12.6	0.45	0.04	10.0	6.3	0.5
n- C_4H_{10}	10.4	3.15	0.70	8.3	21	4.5
iso- C_4H_{10}	8.9	6.1	5.7	7.6	42	37

NOTE: k_1 refers to $CH_3 \cdot + RH \rightarrow CH_4 + R \cdot$.

The reduced activity of ethyl as compared with methyl is obvious but not surprising in view of the lower exothermicity of the ethyl abstractions. In fact, as can be seen from Fig. 7, the experimental values for both radicals lie on a good curve suggesting that at low values of ΔH both radicals have the same activation energy for the same value of ΔH based on some usually accepted figures for C—H bond energy (10). The uncertainty in the bond energies, however, introduces an uncertainty approaching 100% in the C—H bond energy difference for methane and ethane (ΔH). Electron impact methods although subject to criticism have been used to obtain more precise information on such differences (12). It can be seen from Table V that the activation energy difference (ΔE) for methyl and ethyl abstracting from neopentane is 2.6 kcal. It has been suggested that the constant α (in the expression $\Delta E = \alpha \Delta H$) should have a maximum value of 0.5 due to the symmetry of the reaction (11) and this leads to a minimum ΔH of 5.2 kcal. The same is true of the previously observed activation energies for abstraction by methyl from methane (16, 17) and ethane (18, 19), which also differ by about 2.6 kcal. The figure of 5.2 kcal is in excellent agreement with the electron impact value of 5.1 ± 0.7 kcal. Hence the data suggests that α approaches a value of 0.5 at low negative values of ΔH and one assumes that this may be extended to endothermic reactions. The equation of the line is $E = 14.1 + (\Delta H/2)$ (in kcal). The ΔE for methyl and ethyl abstractions from various hydrocarbons varies, but definitely seems to increase with the

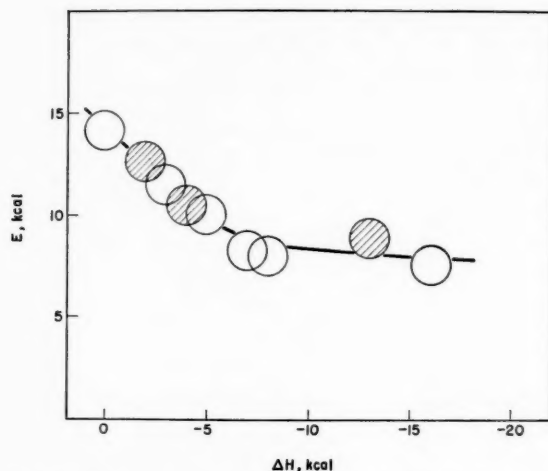


FIG. 7. Activation energy for H atom abstraction vs. ΔH , for CH_3 and C_2D_5 radicals.

strength of the bond broken. Since ΔE is 2.6 kcal for neopentane it should be at least this for ethane. Hence the activation energy for ethyl abstracting from ethane should be at least 14.1 kcal. (This is very close to the corresponding thermally neutral methyl abstraction from methane.) By assuming ΔH for ethane and neopentane to be 3.0 kcal (this is well within the accuracy of the photobromination experiments) and taking ΔH for methane and ethane as 5.2 kcal the following table may be constructed from the above equation.

TABLE VI

Radical abstracting from:	Activation energy in kcal		
	CH_4	C_2H_6	neo- C_5H_{12}
$\text{CH}_3\cdot$	14.1*	11.5*	10.0*
$\text{C}_2\text{H}_5\cdot$	16.7**	14.1	12.6*
neo- $\text{C}_5\text{H}_{11}\cdot$	18.2	15.6	14.1

Values marked * have been experimentally measured and agree closely with the equation. Value marked ** was estimated by the present authors to be greater than 16.0 kcal on the basis of an unsuccessful attempt to measure the activation energy of ethyl- d_5 abstracting from methane. The yield of $\text{C}_2\text{D}_5\text{H}$ at the highest temperature was used with an assumed steric factor of 10^{-3} to calculate an approximate lower limit of the activation energy. Table VI is entirely consistent with the requirement that the activation energy difference between the forward and reverse reactions should equal ΔH .

An estimate is made of the activation energies for neopentyl radical abstractions. If these values are correct they may never be measured experimentally due to the radical decomposition and rearrangement occurring at the temperatures necessary to measure activation energies of this magnitude. There seems to be no reason not to include all alkyl radicals in this treatment since a ΔH of 5.0 kcal seems to make no difference in the methyl and ethyl case. Results with isopropyl and *tert*-butyl radicals are awaited

with interest. If the above argument is correct these radicals should have $\alpha = 0.5$ throughout almost the whole range of their abstraction from alkanes.

The result deduced in an earlier section that in the disproportionation of ethyl radicals C—H bonds break 1.4 times more frequently than C—D bonds is of particular interest. This figure is almost exactly equal to the ratio of C—H and C—D stretching frequencies in C_2H_6 and C_2D_6 (13). There is an empirical rule that in similar molecules corresponding vibrations stand in the same ratio (14). This is extended here to the assumption that the frequency ratio for a certain type of vibration in C_2H_6 and C_2D_6 is the same for a similar vibration in C_2H_5 and C_2D_5 .

$$\frac{R_{C-H \text{ break}}}{R_{C-D \text{ break}}} = \frac{0.139}{0.0985} = 1.41.$$

	ν_1 (cm ⁻¹)	ν_8 (cm ⁻¹)
C—H stretch in C_2H_6	2899	2954
C—D stretch in C_2D_6	2083	2111
Ratio	1.39	1.40

It appears that there is good evidence here to definitely relate the steric factor of the reaction with the vibrational frequency of the reacting bond. There is probably at least one other term in the steric factor but here where the reactions are so similar it may be expected to be about equal in the two cases.

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THE EFFECT OF SOLVENTS UPON EQUILIBRIA, SPECTRA, AND REACTION RATES¹

S. BROWNSTEIN

ABSTRACT

It is shown that the effect of solvent upon a wide variety of equilibria, reaction rates, and spectral shifts may be described by the equation $\log(k_{\text{solvent}}/k_{\text{ethanol}}) = SR$. S is a constant related to the polarity of the solvent and R is a measure of the sensitivity of the system to change in solvent polarity. Tables of S and R are included.

INTRODUCTION

Many attempts have been made to correlate solvent effects with a physical property of the solvent (1-4). Most of these have involved a function of the dielectric constant of the solvent, but refractive index has also been used in an attempt to correlate spectral shifts (5). No satisfactory correlation with a physical property of the solvent could be obtained over an extended range of solvents, or solvent composition in a mixed solvent. This was attributed to specific solvent-solute interaction for some solvents and the ineffectiveness of dielectric constant as a measure of the hydrogen bonding ability of a solvent.

A linear relationship has been observed for the change in reaction rate of closely related reactions as the solvent is varied (6). However, by its nature it is limited to solvolysis reactions and hydroxylic solvents. A four-parameter equation has also been proposed for this group of reactions (7). A similar relationship has been observed in the solvent-dependent shift of certain infrared frequencies (8, 9). A correlation has also been found between solvent effects on solvolysis reactions, described by Y values (6), and ultraviolet spectral shifts, described by Z values (10). Again this cannot be readily extended, as it is formulated, to widely different situations. The success of Kosower's correlation of solvent effects upon solvolysis reactions and ultraviolet spectral shifts suggests the possibility of a semiquantitative correlation of solvent effect upon a wide variety of reactions, equilibria, and spectral shifts. Therefore, it should be possible to predict approximately the effect of changing solvent in a wide variety of cases.

It is the purpose of this paper to propose an equation for correlating solvent effects and to show how well this fits some of the results obtained by a variety of workers. Since the effect of solvent is to change the free energy of the product, activated complex, or excited state, relative to the initial state, a linear free-energy relationship similar to that proposed by Hammett for the reactions of substituted benzenes seems appropriate (11). Absolute ethanol will arbitrarily be chosen as the standard solvent. It appears suitable since much work has been done in this solvent and it is intermediate in dielectric constant and polarity.

Let us assume $\log(k_{\text{solvent}}/k_{\text{EtOH}}) = SR$ where k is a reaction rate, equilibrium constant, or function of a spectral shift. S will be a constant characteristic of any given solvent or solvent mixture. For absolute ethanol it is defined as 0.000 by the above equation, since any other value would require all reactions to have $R = 0.000$. R is a constant characteristic of the sensitivity of a given reaction to solvent effects. The shift of the absorption maximum in 1-ethyl-4-carbomethoxypyridinium iodide (10) was arbitrarily chosen to have

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$R = 1.000$. This reaction was chosen since data is available for a wider range of solvents than with most other reactions. With the choice of one standard solvent and one standard reaction, S and R values may be calculated for any reaction and any solvent. The present discussion is limited to a single temperature and 25°C , or room temperature, has been chosen. Although relative solvent polarities, and hence S values, will change with temperature the effect is probably small, since activation energies for a given reaction in various solvents are usually quite similar (6).

Reaction rates and equilibrium constants are exponentially proportional to the difference in free energy between initial and final states while shifts in frequency are directly proportional to energy differences. Therefore for shifts in spectral absorption

$$k = e^{\tilde{\nu}_{\max \text{ solv}}/\tilde{\nu}_{\max \text{ EtOH}}}$$

Then

$$\begin{aligned} SR &= \log \frac{e^{\tilde{\nu}_{\max \text{ solv}}/\tilde{\nu}_{\max \text{ EtOH}}}}{e^{\tilde{\nu}_{\max \text{ EtOH}}/\tilde{\nu}_{\max \text{ EtOH}}}} \\ &= \frac{\tilde{\nu}_{\max \text{ solv}}}{\tilde{\nu}_{\max \text{ EtOH}}} - \frac{\tilde{\nu}_{\max \text{ EtOH}}}{\tilde{\nu}_{\max \text{ EtOH}}} \\ &= \frac{\tilde{\nu}_{\max \text{ solv}} - \tilde{\nu}_{\max \text{ EtOH}}}{\tilde{\nu}_{\max \text{ EtOH}}} \end{aligned}$$

In cases where the appropriate measurements have not been made in absolute ethanol as solvent, and it is not feasible to do them, the following procedure may be used.

$$\begin{aligned} S_1R &= \log \left(\frac{k_{s1}}{k_{\text{EtOH}}} \right) = \log k_{s1} - \log k_{\text{EtOH}} \\ S_2R &= \log \left(\frac{k_{s2}}{k_{\text{EtOH}}} \right) = \log k_{s2} - \log k_{\text{EtOH}} \end{aligned}$$

Therefore

$$R(S_1 - S_2) = \log k_{s1} - \log k_{s2}$$

and

$$R = \frac{\log k_{s1} - \log k_{s2}}{S_1 - S_2}$$

It is desirable to have results in several solvents grouped into two equal sets and use

$$R = \frac{\sum \log k_{s1} - \sum \log k_{s2}}{\sum S_1 - \sum S_2}$$

In cases where k is a frequency this still does not remove the necessity of a measurement in absolute ethanol since

$$\log k_{s1} = \log e^{\tilde{\nu}_{\max S_1}/\tilde{\nu}_{\max \text{ EtOH}}} = \frac{\tilde{\nu}_{\max S_1}}{\tilde{\nu}_{\max \text{ EtOH}}}$$

and

$$R = \left\{ \frac{\tilde{\nu}_{\max S_1} - \tilde{\nu}_{\max S_2}}{\tilde{\nu}_{\max \text{ EtOH}}} \right\} / (S_1 - S_2)$$

For these cases the data were plotted and the value found for the frequency at S equals zero was used for $\tilde{\nu}_{\max \text{ EtOH}}$.

EXPERIMENTAL

The data of Kosower (10) were used to determine 58 S values. In those cases where concentration of the pyridinium salt affected the spectral shift, the results were extrapolated to infinite dilution. Using these S values, R values were calculated for nine

TABLE I

S values

Aqueous solutions		% Dioxane	S	Pyridine-benzene	S
% Ethanol	S	100	-.179	1:9	-.1913
100	0	90	-.0384	1:99	-.1992
98	.00825	85	-.0056	Chloroform-acetic acid	S
96	.0154	80	.0071	1:1	-.0420
95	.0201	75	.0268	Chloroform-iso-octane	S
92	.0302	70	.0413	1:1	-.1240
90	.0366	60	.0766	Propanol-toluene	S
85	.0525	50	.0947	1:9	-.1053
80	.0650	40	.1108	Acetic acid-formic acid	S
75	.0761	30	.1250	% Acetic acid	S
70	.0848	20	.1369	75	.0518
60	.0880	10	.1464	50	.0778
50	.1028	% 2-Propanol	S	25	.0875
45	.1102	100	-.0413	10	.1085
40	.1177	95	-.0032	Dioxane-formic acid	S
37.5	.1219	90	.0234	% Dioxane	S
35	.1255	80	.0546	60	.0378
30	.1325	% Formic acid	S	40	.0678
25	.1376	100	.1139	20	.0648
20	.1417	95	.1170	Pure solvents	S
15	.1455	90	.1185	1-Propanol	-.0158
10	.1490	80	.1212	1-Butanol	-.0240
5	.1515	66 2/3	.1250	Formamide	.0463
% Methanol	S	50	.1303	Acetonitrile	-.1039
100	.0499	33 1/3	.1390	Methyl cyclopropyl	
97.5	.0560	25	.1430	ketone	-.1788
95	.0615	14.3	.1470	Ethylene glycol	.0679
92.5	.0668	% Pyridine	S	Water	.1540
90	.0740	100	-.1970	Ethyl acetate	-.210
87.5	.0782	95	-.1248	Isopropyl ether	-.229
85	.0849	90	-.0830	Ether	-.277
80	.0674	80	-.0330	n-Butyl ether	-.286
77	.0777	% Dimethyl formamide	S	Triethylamine	-.285
72	.0850	100	-.1416	Chloroform	-.2000
60	.0983	90	-.0762	Methylene chloride	-.1890
50	.1116	80	-.0262	Gas phase	-.556
40	.1234	% t-Butanol	S	Tetrachloroethylene	-.263
30	.1334	100	-.1047	Carbon tetrachloride	-.245
20	.1409	95	-.0392	Methyl iodide	-.170
10	.1480	90	.0097	Carbon disulphide	-.240
% Acetone	S	80	.0460	Nitromethane	-.134
100	-.1748	Acetic acid	S	Methylene bromide	-.095
99	-.1499	100%	.0050	Sym. tetrachloro-	
95	-.0848	.50MH ₂ O	.0176	ethane	-.083
93	-.0607	2.00MH ₂ O	.0326	Bromoform	-.042
90	-.0388	4.00MH ₂ O	.0454	Ethylene dichloride	-.151
85	-.0111	8.00MH ₂ O	.0621	Methylene iodide	-.043
80	.0136	16.00MH ₂ O	.0840	n-Heptane	-.337
75	.0316	60%	.0990	n-Hexane	-.337
70	.0449	50%	.1105	Cyclohexane	-.324
65	.0591	40%	.1210	Nitrobenzene	-.218
60	.0744	25%	.1359	Mesitylene	-.217
50	.0956	Other solutions		Anisole	-.214
40	.1119	Methanol-iso-octane	S	Chlorobenzene	-.182
30	.1258	% Methanol by volume	S	Bromobenzene	-.164
25	.1316	95	.0477	Toluene	-.237
20	.1378	90	.0456	Benzene	-.215
10	.1467	85	.0435	ψ Cumene	-.245
5	.1526	80	.0420	Aniline	.001
				Pyrrrole	.012

*Weight % is meant unless otherwise mentioned.

reactions and these in turn were used to calculate a total of 158 *S* values. These *S* values were then used to determine 78 *R* values. These figures are given in Tables I and II. This does not constitute an exhaustive survey of the literature but is sufficient to show the range of values which can be expected.

A minimum of nine points were used to determine *R* values of reactions which were subsequently utilized to determine further *S* values. If the average deviation for these reactions was large, results from two or three reactions were averaged to obtain the additional *S* values. For the carbonyl absorption of acetone, dimethyl formamide, and methyl acetate in the infrared, data were obtained for additional solvents in this laboratory using a Perkin-Elmer model 21 spectrophotometer with a rock salt prism. It was calibrated immediately before use.

TABLE II
R values

Reaction	<i>R</i>	Deviation	<i>n</i>	Reference
U.V. absorption of 1-methyl-4-carbomethoxypyridinium iodide	* .963	.088	19	(10)
U.V. absorption of 1-ethyl-4-cyanopyridinium iodide	1.076	.047	6	(10)
U.V. absorption of pyridine-1-oxide	.224	.092	12	(10)
Solvolysis of <i>t</i> -butyl chloride	*35.89	1.07	17	(3, 6)
Solvolysis of <i>t</i> -butyl bromide	29.9	4.1	20	(14)
Solvolysis of benzhydryl chloride	22.8	6.3	19	(15)
Solvolysis of α -phenylethyl chloride	29.4	4.5	32	(14)
Solvolysis of α -phenylethyl bromide	26.6	3.7	20	(14)
Solvolysis of benzhydryl bromide	20.0	8.6	5	(15)
" of trityl fluoride	25.4	5.0	6	(7)
" of <i>p</i> -nitrobenzoyl chloride	8.3	2.3	5	(16)
" of <i>p</i> -nitrobenzoyl fluoride	20.2	5.6	7	(16)
" of benzoyl chloride	13.5	2.4	9	(16)
" of benzoyl fluoride	23.3	3.2	7	(16)
" of acetic anhydride	18.6	6.1	7	(17)
C=O absorption of acetone	*-.036	.021	10	(8)
C=O absorption of dimethyl formamide	-.045	.025	10	(8)
C=O absorption of methyl acetate	*-.057	.026	9	(8)
U.V. absorption of 2,6-dimethyl-4-seleno- γ -pyran	.822	.226	14	(18)
C=O absorption of cyclohexanone	-.021	.012	22	(8)
C=O " of benzophenone	-.045	.011	24	(8)
C=O " of acetophenone	-.020	.010	24	(8)
C=O " of acetyl chloride	-.017	.007	21	(8)
1867 cm ⁻¹ absorption of ethylene carbonate	-.054	.009	20	(8)
1758 cm ⁻¹ absorption of ethylene carbonate	.028	.014	20	(8)
N-H absorption of pyrrole	-3.19	0.81	17	(19)
Solvolysis of methane sulphonyl chloride	11.0	0.8	9	(20)
Solvolysis of ethyl chloroformate	9.9	0.5	12	(20)
Asymmetric N-H absorption of aniline	*-.079	.017	10	(19)
Symmetric N-H absorption of aniline	*-.194	.048	10	(19)
Asymmetric O-H stretch of water	-1.15	.25	11	(19)
Symmetric O-H stretch of water	-1.03	.22	11	(19)
B-H stretch of decaborane	-.059	.005	9	(19)
O-H stretch of phenol	-.484	.073	8	(19)
Racemization of 2-nitro-6-carboxy-2'-methoxybiphenyl	No correlation		6	(21)
Racemization of 2-nitro-6-carboxy-2'-ethoxybiphenyl	No correlation		6	(21)
Chemical shift difference of extra ring protons of benzyl alcohol	20.9	3.1	13	(22)
S=O frequency of dimethyl sulphoxide	-.140	.032	19	(23)
Phenyl frequency of diphenyl sulphoxide	-.026	.004	17	(23)
S=O frequency of diphenyl sulphoxide	-.063	.011	19	(23)
S=O frequency of thionyl chloride	-.037	.007	13	(23)
P=O frequency of phosphorous oxychloride	-.073	.015	10	(23)
Susceptibility corrected chemical shift of propargyl bromide CH ₂	2.86	.27	8	(24)

TABLE II (concluded)

Reaction	R	Deviation	n	Reference
Susceptibility corrected chemical shift of propargyl bromide CH	3.32	.23	7	(24)
Chemical shift difference of CH ₂ and CH protons of propargyl bromide	-.86	.07	7	(24)
C≡H stretch of propargyl bromide	-.044	.005	8	(24)
High frequency P=O stretch of dimethyl hydrogen phosphonate	-.099	.010	17	(23)
Low frequency P=O stretch of dimethyl hydrogen phosphonate	-.071	.007	17	(23)
Trans N=O stretch of methyl nitrite	-.051	.011	11	(23)
Third harmonic OH band of CH ₃ OH	-.048	.018	9	(25)
2nd OH overtone of phenol	-.203	.034	10	(26)
N—N band of dimethyl nitrosamine	.130	.028	14	(23)
Pseudo dimer N=O band of nitrosamine	No correlation		9	(23)
N=O band of dimethyl nitrosamine	-.071	.014	9	(23)
Trans N=O stretch of isopropyl nitrate	-.062	.017	11	(23)
Cis N=O stretch of isopropyl nitrate	-.016	.005	11	(23)
Rate of reaction of aniline with ω -bromoacetophenone	4.30	2.35	7	(27)
$\pi \rightarrow \pi^*$ transition of nitrobenzene	-.075	.035	5	(28)
$n \rightarrow \pi^*$ transition of nitromethane	.050	.022	7	(28)
$n \rightarrow \pi^*$ transition of crotonaldehyde	.26	.08	5	(28)
$n \rightarrow \pi^*$ transition of acetone	.097	.037	7	(28)
λ_{max} of phenol blue	*-.281	.081	15	(29)
5000 Å absorption of lycopene	.166	.088	11	(29)
4800 Å absorption of lycopene	.146	.060	9	(29)
4500 Å absorption of lycopene	.126	.050	9	(29)
Absorption of phenolphthalein	.192	.057	6	(29)
Absorption of <i>p</i> -rosaniline hydrochloride	.222	.240	9	(29)
Keto-enol equilibrium of ethyl acetoacetate	-3.48	3.48	14	(30)
Long wavelength absorption of mesityl oxide	.129	.045	9	(10)
Absorption of 2-methyl-4,6-diphenylpyridinium N ⁺ N Betaine	.273	.108	10	(31)
Pyridine + ethyl iodide yields pyridinium iodide (rate)	3.01	1.87	7	(32)
Short wavelength absorption of mesityl oxide	No correlation		9	(10)
Proton resonance shift of water between vapor and solution	3.78	1.08	10	(33)
Fluorine resonance shift of benzotrifluoride	No correlation		8	(34)
Fluorine resonance shift of 1,2-di-fluorotetra-chloroethane	No correlation		8	(34)
Fluorine resonance shift of 1-fluoropentane	3.46	2.16	6	(34)
Reaction of trimethylamine and <i>o</i> -nitrobenzylchloride	No correlation		7	(35)
Reaction of trimethylamine and <i>m</i> -nitrobenzylchloride	No correlation		7	(35)
Reaction of trimethylamine and <i>p</i> -nitrobenzylchloride	No correlation		7	(35)
Decomposition of azodicarbonate ion	9.86	.06	7	(36)
Reaction of methyl iodide and silver nitrate	-2.82	1.72	6	(37)
1st dissociation constant of succinic acid	12.4	2.0	15	(38)
2nd dissociation constant of succinic acid	18.4	2.7	15	(38)
1st dissociation constant of azelaic acid	29.4	2.4	12	(38)
2nd dissociation constant of azelaic acid	33.8	2.6	12	(38)
Isomerization of <i>cis</i> -azobenzene	-1.6	0.8	9	(39, 40)
Racemization of <i>tris</i> -oxalato-chromium III	19.7	2.8	12	(41)

DISCUSSION

There is found to be a good fit of the proposed equation to the experimental data. Therefore, there is probably a characteristic of solvents, described here by *S* values, which is responsible for solvent effects in a wide variety of situations. However, this type of correlation necessarily averages out individual differences in solvents and reactions so it would be dangerous to attribute too much theoretical significance to the individual numbers. It obviously will not apply to measurements where there is a unique interaction between the solvent and the species which is being measured. Such a situation occurs with infrared spectral shifts when there is hydrogen bonding between the solvent

and some functional group of the substance whose spectrum is being determined. It also occurs when the solvent is able to complex with one of the species in a reaction whose rate is being determined. This type of correlation should nevertheless prove quite useful in transposing data, primarily spectroscopic, from one solvent system to another.

For the rates of 14 solvolysis reactions the average deviation from the individual R values was 19.4% for rates differing by up to 10,000 times. The R values for the individual reactions were all positive and varied between 9.9 and 35.9. For 32 infrared absorptions the average deviation from the individual R values was 27%. All R values were negative and ranged between -3.19 and $-.016$ except for two positive values and one case which did not fit the equation. These numbers correspond to a slight solvent shift and the experimental accuracy in determining the solvent shifts usually limited the accuracy with which the data fitted the equation.

For the spectral shifts of 15 ultraviolet absorptions the average deviation from the individual R values was 34%. There was no correlation in two instances. The R values were positive and ranged between .05 and 1.08 except for two negative values. It has been suggested that $\pi \rightarrow \pi^*$ transitions are affected differently by solvent change than $n \rightarrow \pi^*$ transitions (12). This can be stated more quantitatively by noting that $\pi \rightarrow \pi^*$ transitions are likely to have negative R values. The solvent corrections for Woodward's rules can also be stated in terms of R values (13). They correspond to saying the transitions usually have an R value of about 0.10, although chloroform does not seem to fit this scheme very well.

Magnetic-susceptibility-corrected solvent shifts of nuclear resonance spectra are also correlated by the same equation. The average deviation in individual R values for five proton resonance solvent shifts is only 13.6%. Little correlation is found with fluorine resonance shifts.

This type of correlation should be useful in correcting literature values of data in some solvent system to the system which an investigator finds convenient in his own work.

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THE FLUORINE RESONANCE SPECTRUM OF PERCHLORYL FLUORIDE¹

S. BROWNSTEIN

ABSTRACT

The first instance of observable spin-spin coupling with a chlorine nucleus is found in the fluorine resonance of perchloryl fluoride. The explanations of this, and of the very large chemical shift, are given.

When a nucleus of non-zero spin is bonded directly, or with a few intervening atoms, to another nucleus of non-zero spin, coupling of the two nuclear spins occurs via the bonding electrons. If the spin-coupled nuclei are magnetically non-equivalent, the spin coupling manifests itself by a splitting of the observed nuclear resonance peaks (1, Chap. 8). When a nucleus of spin $1/2$ is coupled to a nucleus with spin greater than $1/2$, spin coupling is not always observed in the resonance spectrum of the nucleus with spin $1/2$. This is attributed to a rapid relaxation of the nucleus with spin greater than $1/2$ due to interaction of its quadrupole moment with an unsymmetric electric field gradient. One would expect to see spin coupling when there is spherical symmetry about the nucleus of spin greater than one half, and this is observed (2). If the symmetry is less, the individual lines broaden and eventually coalesce into a single sharp line when the relaxation is rapid.

No examples have been reported of observable spin coupling of nuclei with chlorine, but sharp single peaks are always observed. Both chlorine-35 and chlorine-37 have spin $3/2$ and appreciable quadrupole moments. Since chlorine is quite electronegative, unsymmetric bonds are to be expected in most of its compounds and rapid relaxation of the chlorine nuclear spin occurs. Three oxygens and a fluorine are tetrahedrally arranged about a central chlorine in perchloryl fluoride and the compound has no observable dipole moment (3). Relaxation of the chlorine nuclear spin should not be too rapid in this compound.

The fluorine resonance spectrum of perchloryl fluoride is shown in Fig. 1. It has a

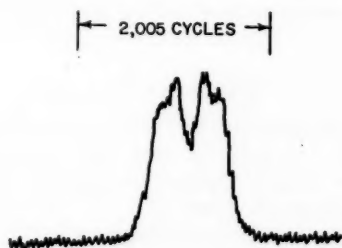


FIG. 1. Fluorine resonance of perchloryl fluoride.

chemical shift of 320 p.p.m. to low field from the fluorine resonance in trifluoroacetic acid. The splitting between the two partially resolved lines is 310 cycles and the extrapolated line width, at half the height, for each line is 430 cycles. The signal is very weak requiring

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40 decibels more of radio-frequency power to obtain the same signal intensity as that of trifluoroacetic acid.

A correlation of chemical shift with the electronegativity of the atom or group to which fluorine is bonded has been demonstrated (4). The shift to low field is greatest the lower the electron density about fluorine, with the spherically symmetric fluoride ion occurring at highest field. The fluorine resonance shift in perchloryl fluoride is to lower field than any compound of fluorine, except for molecular fluorine. The lack of dipole moment for perchloryl fluoride suggests that the electronegativity of the perchloryl group approaches that of fluorine. Therefore the chemical shift is in agreement with previous observations.

Four lines of equal intensity are to be expected in the spectrum of a nucleus spin coupled to one other of spin $3/2$. Since both stable isotopes of chlorine have spin $3/2$ two sets of four lines will be expected with $J_{\text{Cl}^{35}}/J_{\text{Cl}^{37}} = \mu_{\text{Cl}^{35}}/\mu_{\text{Cl}^{37}} = .821/.683$ (1, p. 188).

The relative intensities will be three to one. Combining the individual spectra gives a composite spectrum in which the intensity between the outside peaks is greater than between the center ones. This is illustrated in Fig. 2 for triangular peaks. A Gaussian

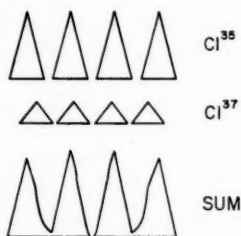


FIG. 2. Effect of isotopic composition upon the spectrum.

line shape would probably accentuate this. Possibly for this reason only two poorly resolved peaks are actually observed.

The lines of perchloryl fluoride have a width of 430 cycles whereas at the same sweep rate the resonance of trifluoroacetic acid is immeasurably narrow. Therefore considerable broadening of the fluorine resonance is occurring due to rapid relaxation of the chlorine nuclear spin.

EXPERIMENTAL

Perchloryl fluoride was obtained from Pennsalt Chemicals Corporation, and used without further purification. The gas was condensed under vacuum into a 5-mm O.D. Pyrex tube which was then sealed. Upon warming to room temperature, a colorless mobile liquid remained in the sample tube.

The spectra were run on a Varian Associates high resolution nuclear magnetic resonance spectrometer Model V4300C operating at 56.4 Mc. The spectra were calibrated using audio side bands (5) counted with a Hewlett Packard Model 521C frequency counter. Since the observed chemical shift was beyond the normal sweep range of the instrument, the magnet current was varied after the instrument was calibrated. Because of hysteresis in the electromagnet, the chemical shift obtained in this manner will only be accurate within about 5 p.p.m. A radio-frequency power level of 50 db below $1/2$ watt was required to produce an adequate signal. Variation of the power about this level gave no indication of saturation of the signal.

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THE PREPARATION OF CYCLIC PEROXIDES AND THEIR DECOMPOSITION IN SOLUTION¹

K. E. RUSSELL

ABSTRACT

The cyclic dimers of sebacyl, dodecanedioyl, and tetradecanedioyl peroxide have been prepared, together with high yields of the corresponding high molecular weight polymeric peroxides. The decomposition of these peroxides in styrene and benzene solution has been studied. The results show that if diradicals are formed in the breakdown of the cyclic peroxides, they undergo self-termination before reacting with a significant number of styrene molecules. In the presence of low concentrations of 1,1-diphenyl-2-picrylhydrazyl (DPPH) in benzene solution, self-termination of diradicals is preferred to reaction with the hydrazyl.

INTRODUCTION

The main objective of this investigation was to study the reactions of diradicals obtained by the thermal breakdown of cyclic peroxides. Previous work (1, 2) has shown that phthalyl peroxide may be readily prepared by the reaction of phthalyl chloride with sodium peroxide, but that its decomposition in solution may be complex (2, 3). It was thus not possible to reach firm conclusions concerning the reactions of diradicals from studies involving this aromatic peroxide. Some cyclic aliphatic peroxides have now been prepared using the same experimental method. Attempts were made to isolate succinyl, adipyl, suberyl, azelalyl, sebacyl, dodecanedioyl, and tetradecanedioyl peroxides, but low molecular weight cyclic peroxides were only obtained in the last three cases. Polymeric peroxides of high molecular weight were always obtained as the major reaction products.

The decomposition of the cyclic and linear peroxides in benzene solution was studied by direct analysis in order to show that there is no fundamental difference in the primary step of the breakdown. Measurements were made of the rate of polymerization of styrene using the various peroxides as initiators to determine to what extent the radical intermediates grow to give high molecular weight polystyrene. The decomposition of the peroxides in benzene solutions of 1,1-diphenyl-2-picrylhydrazyl (DPPH) was studied to give information concerning the reactions of the radical intermediates with DPPH.

EXPERIMENTAL

Materials

Chloroform was treated with concentrated sulphuric acid to remove alcohol and was washed twice with distilled water. Reagent grade (Fisher) benzene was used for the kinetic studies. Styrene was distilled at 15 mm pressure and subjected to two bulb-to-bulb distillations on the high vacuum line. DPPH was prepared by the method of Goldschmidt and Renn (4); it was heated *in vacuo* to 90° for 1 hour to remove complexed solvent. Succinyl, adipyl, sebacyl, and hexanoyl chlorides were Eastman Kodak materials.

Suberic, azelaic, dodecanedioic, and tetradecanedioic acids were converted to the corresponding acid chlorides by reaction with thionyl chloride. Thionyl chloride (2.4 moles per mole of acid) was used and the reaction was allowed to proceed for 3 days at 40°; excess thionyl chloride was distilled off at reduced pressure. The light yellow product was treated with activated charcoal. (This modification of the usual method was suggested by R. F. Liming, Distillation Products Industries.) The purity of the acid chlorides was

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shown to be greater than 98.5% by allowing them to react with 6 *N* sodium hydroxide, adding 6 *N* hydrochloric acid equivalent to the sodium hydroxide, and determining the hydrochloric and dibasic acids present.

Preparation of the Peroxides

The peroxides were prepared by stirring a dilute aqueous solution of sodium peroxide with a dilute chloroform solution of the acid chloride. In a typical preparation, 20 g of disodium hydrogen phosphate hexahydrate and 0.01 mole of sodium peroxide were added to 110 ml of water at 0° C. A solution of 0.015 mole of acid chloride in 250 ml of chloroform was added and the mixture stirred vigorously. Further quantities of sodium peroxide, up to a total of 0.025 mole, were added over a period of 20 minutes. Stirring was continued for a further 30 minutes.

The chloroform layer was separated and washed twice with water, and the chloroform was evaporated with a stream of dry air at room temperature. The white solid obtained was extracted twice with low-boiling petroleum ether.

Significant yields of low molecular weight peroxide soluble in petroleum ether were obtained only in the cases of sebacyl, dodecanedioyl, and tetradecanedioyl peroxides. These materials were purified by recrystallization from petroleum ether and dried *in vacuo* at room temperature. Molecular weights were determined by measurement of the depression of the freezing point of pure benzene, and peroxide contents were determined by the method of Wagner, Smith, and Peters (5). Sebacyl peroxide: yield 4–6%, m.p. 19–21°. Anal. Calc. for $C_{10}H_{18}O_4$: C, 60.0; H, 8.06; —O—O—, 16.0. Found: C, 60.16, 60.22; H, 8.07, 8.06; —O—O—, 15.8%. Mol. wt. 360, 370. Dodecanedioyl peroxide: yield 5–6%, m.p. 32–35°. Anal. Calc. for $C_{12}H_{20}O_4$: C, 63.15; H, 8.77; —O—O—, 14.0. Found: C, 63.17, 63.26; H, 8.78, 8.97; —O—O—, 13.8, 13.7%. Mol. wt. 429, 473. Tetradecanedioyl peroxide: yield 7–9%, m.p. 43–46°. Anal. Calc. for $C_{14}H_{24}O_4$: C, 65.56; H, 9.38; —O—O—, 12.5. Found: C, 65.54, 65.58; H, 9.65, 9.53; —O—O—, 12.1%. Mol. wt. 462.

In the attempted preparation of succinyl peroxide a low yield of chloroform-insoluble peroxide was obtained and very little peroxide remained in the chloroform layer even before evaporation. With other preparations the major product was a peroxide which was insoluble in petroleum ether. Molecular weight determination by depression of the freezing point of benzene indicated values greater than 3000; intrinsic viscosities of chloroform solutions of sebacyl, dodecanedioyl, and tetradecanedioyl peroxides varied between 0.3 and 0.5. These high molecular weight peroxides will be referred to as polymeric peroxides and individual peroxides as polysebacyl peroxide, etc. *When dry, polymeric peroxides explode on scratching or on heating. The sensitivity to percussion and the vigor of the explosion increase with the peroxide content of the polymeric peroxide.* Polyadipyl peroxide: yield 50%, m.p. 118–119° decomp. Polysuberyl peroxide: yield 75%, m.p. 116–118° decomp. Anal. Calc. for $C_8H_{12}O_4$: —O—O—, 18.6. Found: —O—O—, 18.3%. Polyazelayl peroxide: yield 70%, m.p. 104–105° decomp. Anal. Calc. for $C_9H_{14}O_4$: —O—O—, 17.2. Found: —O—O—, 17.0%. Polysebacyl peroxide: yield 85%, m.p. 112–113° decomp. Anal. Calc. for $C_{10}H_{18}O_4$: C, 60.0; H, 8.06; —O—O—, 16.0. Found: C, 60.12, 60.22; H, 8.07, 7.95; —O—O—, 15.9, 15.8%. Polydodecanedioyl peroxide: yield 80%, m.p. 108–109°. Anal. Calc. for $C_{12}H_{20}O_4$: —O—O—, 14.0. Found: —O—O—, 13.7%. Polytetradecanedioyl peroxide: yield 80%, m.p. 108–110°. Anal. Calc. for $C_{14}H_{24}O_4$: —O—O—, 12.5. Found: —O—O—, 11.9%.

Hexanoyl peroxide was prepared by the above method. Anal. Calc. for $C_{12}H_{22}O_4$: —O—O—, 13.9. Found: —O—O—, 13.4%. Mol. wt. 219.

Infrared spectra were taken of the low molecular weight and polymeric sebacyl, dodecanedioyl, and tetradecanedioyl peroxides in chloroform solution using a Perkin-Elmer Model 21 spectrometer.

Decomposition Studies

The rates of breakdown of the peroxides in benzene and styrene solutions were determined by peroxide analysis. For styrene as solvent, about 0.04 g of peroxide was weighed and introduced into a reaction tube. Approximately 4 g of styrene was distilled into the tube, and after it was sealed off, the tube was placed in a bath at 60° for 1 hour or 2 hours. The remaining peroxide was then estimated (5). For benzene as solvent, the solutions were degassed twice before being placed in the bath at 60°.

In the polymerization studies, solutions of peroxide in styrene were made up as described above, and the polymerization allowed to proceed at 60° for 2 hours. The high molecular weight polystyrene was precipitated in methanol, filtered, and dried *in vacuo* at 60°.

The rates of disappearance of DPPH were studied using benzene solutions which were approximately 0.0004 *M* in DPPH and 0.005 *M* in peroxide. The solutions were degassed and were heated to 60° for periods of 20 minutes. Readings of optical density were taken at a solution temperature of 20° using a Fisher electrophotometer with a 650 m μ filter. The optical densities of a series of DPPH solutions of known concentration were also determined.

RESULTS AND DISCUSSION

The Structures of the Peroxides

The major product of the reaction between a dibasic acid chloride and sodium peroxide under the experimental conditions used in this work is a polymeric peroxide. Good yields of polyadipyl, polysuberyl, polyazelayl, polysebacyl, polydodecanedioyl, and polytetradecanedioyl peroxides were obtained. The average molecular weights of the polymeric peroxides are probably between 5000 and 10,000. They are almost certainly linear polymers.

Small yields of low polymers of sebacyl, dodecanedioyl, and tetradecanedioyl peroxides were isolated. Analytical data and molecular weight determinations suggest that these low polymers are cyclic dimers. It is possible that the products are mixtures of low polymers, e.g., cyclic monomer, dimer, and trimer. However, fractional crystallization did not appreciably affect the melting points of the products and it is probable that the peroxides are largely, if not completely, cyclic dimers. Confirmatory evidence for the nature of the low molecular weight products is provided by their infrared spectra. The spectra of corresponding low and high molecular weight products are identical except for slight differences in the intensities of some bands. This indicates that similar structural units are present in the dimer and polymer. There is no absorption in the O—H stretching frequency region in any of the spectra; the cyclic dimer is therefore not seriously contaminated by low molecular weight linear peroxides.

The production of cyclic dimer instead of monomer in the case of sebacyl peroxide is not surprising in view of the strain normally involved in 12-membered rings. Overberger and Lapkin (6) obtained the cyclic dimer, 3,12,15,24-tetraphenyl-1,2,13,14-tetraaza-1,13-cyclotetracosatetradiene, when they attempted to prepare the monomeric 12-membered ring compound. A dimer was also formed when they attempted to prepare the corresponding 14-membered ring compound. In the present work it was hoped that the 16-membered

ring of monomeric tetradecanedioyl peroxide would be formed more readily, but the molecular weight evidence indicates that formation of dimer is preferred to that of monomer.

Decomposition of the Peroxides in Solution

The thermal decomposition of the peroxides in benzene and styrene solution was studied by peroxide analysis. The peroxides investigated were the cyclic dimers and the high molecular weight linear polymers of sebacyl, dodecanedioyl, and tetradecanedioyl peroxide. These six peroxides all decompose at rates within the range 5.5 to 8.5%/hour in the two solvents at 60°. Since the cyclic peroxides decompose at approximately the same rates as the linear peroxides, it is reasonable to assume that homolytic cleavage of the peroxide link occurs as the initial step in both cases. The radicals so formed may eliminate carbon dioxide. Thermal decomposition of the polymeric peroxides gives rise to monoradicals and decomposition of the cyclic peroxides leads to diradicals.

The Peroxides as Initiators for the Polymerization of Styrene

The three cyclic dimers and their long-chain linear analogues were used as initiators for the polymerization of styrene at 60°. The measured rates of polymerization were converted to rates of initiation R_i by means of the relationship (7)

$$[1] \quad R_p^2 = 3 \times 10^{-2} R_i.$$

In this work concentrations are expressed in moles/liter and time in seconds; for the peroxides, concentrations are given in moles/liter of monomer units. Values of $R_i/(I)$, where (I) is the concentration of peroxide, are given in Table I.

TABLE I
Rates of initiation of polymerization of styrene and rates of disappearance of DPPH at 60°

	$10^6 R_i/(I) \text{ sec}^{-1}$	$10^6 R_{\text{DPPH}}/(I) \text{ sec}^{-1}$
Polysebacyl peroxide	8.0	12.1
Sebacyl peroxide (cyclic dimer)	0.22	0.5
Polydodecanedioyl peroxide	7.9	11.0
Dodecanedioyl peroxide (cyclic dimer)	0.21	0.35
Polytetradecanedioyl peroxide	8.2	11.4
Tetradecanedioyl peroxide (cyclic dimer)	0.37	0.6
Hexanoyl peroxide	13.8	18

The three polymeric peroxides have a value of $R_i/(I)$ of $8 \times 10^{-6} \text{ sec}^{-1}$ within experimental error. The polymeric peroxides differ only in the number of methylene groups joined together in their repeating units, and unless this number is very small, significant differences between the rates for the three peroxides would not be expected. The value of $R_i/(I)$ for hexanoyl peroxide, a simple linear peroxide, is $13.8 \times 10^{-6} \text{ sec}^{-1}$.

The rates of initiation of polymerization of styrene are very much lower when the cyclic dimers are used as initiators. The maximum rate is observed with tetradecanedioyl peroxide and this is only 4.5% of the rate observed with the corresponding polymeric peroxide. If the cyclic dimers decompose to produce diradicals, these diradicals undergo self-termination before they add on a significant number of styrene units. Other workers have reached a similar conclusion on the basis of theoretical and experimental studies. Zimm and Bragg (8) predicted that even large polystyryl diradicals would undergo self-termination more rapidly than addition of a styrene monomer unit. Tobolsky and Russell

(9) showed that the photochemical breakdown of a cyclic disulphide in styrene gave very little high molecular weight polystyrene, in contrast with the result obtained using a linear disulphide. Overberger and Lapkin (6) observed that the thermal decomposition of a 24-membered ring azo compound in styrene gave a relatively low yield of high polymer, and Cohen *et al.* (10) observed that a 6-membered ring azo compound behaved in a similar manner.

In previous studies it was not clear whether the small amount of high polymer formed arose from the growth of diradicals or of monoradicals originating from an impurity. This point can be investigated by comparing the degree of polymerization of the polystyrene produced by a cyclic peroxide with that predicted by the equation (11)

$$[2] \quad \frac{1}{P_n} = C_m + \frac{K_t}{K_p^2} \times \frac{R_p}{[M]^2}.$$

This relationship applies to initiators which produce monoradicals and which do not undergo chain transfer with polystyryl radicals. P_n is the number average degree of polymerization, C_m is the chain transfer constant for styrene, K_t is the termination rate constant, K_p is the propagation rate constant, and $[M]$ is the concentration of styrene. For samples of polystyrene produced using the three cyclic peroxides as initiators, the experimental and calculated values of P_n are very close to one another (see Table II).

TABLE II
Experimental and calculated degrees of polymerization of polystyrene

	Experimental DP	Calculated DP
Sebacyl peroxide (cyclic dimer)	4460	4100
Dodecanedioyl peroxide (cyclic dimer)	3400	3370
Tetradecanedioyl peroxide (cyclic dimer)	3360	3310

Johnson and Tobolsky (12) have pointed out that polystyrene produced by diradicals which fail to undergo self-termination will have a much larger degree of polymerization than that predicted by the above relationship. The small amount of polystyrene produced when the cyclic peroxides are used as initiators therefore originates from a monoradical-producing compound, which is probably a linear peroxide present as impurity in the cyclic dimer. Diradicals formed in the breakdown of the cyclic dimers appear to have a negligible chance of growing to high polymer.

Decomposition of Peroxides in the Presence of DPPH

DPPH has been used to measure the rate of formation of free radicals in the thermal decomposition of benzoyl peroxide (13). The decomposition of the cyclic peroxides in the presence of DPPH was investigated to determine whether self-termination of diradicals occurred before they could react with DPPH. The linear polymeric peroxides and hexanoyl peroxide were used as standards of comparison. The results obtained for $R_{\text{DPPH}}/(I)$, where R_{DPPH} is the rate of disappearance of DPPH, are given in Table I. The reactions were zero order with respect to DPPH in the concentration range studied. The values of $R_{\text{DPPH}}/(I)$ for the polymeric peroxides are almost 50% greater than the values of $R_1/(I)$. This difference is not necessarily significant as there is some uncertainty in the choice of constant for equation (1) and the experimental error in the DPPH work may be as high as 10%.

The cyclic peroxides give very low values of $R_{\text{DPPH}}/(\text{I})$. The observed rates may well be due to the reaction of DPPH with monoradicals from a small amount of linear peroxide present in the cyclic dimers. Diradicals from the cyclic peroxides thus undergo self-termination in preference to reaction with DPPH.

The high rate of self-termination of large diradicals is of importance in discussing the mechanism of the thermal polymerization of styrene. It appears likely that diradicals are formed in pure styrene (14), and that some of them have a sufficient lifetime to react with a further molecule of styrene (14) or with DPPH (15). This is only possible for small diradicals containing two styrene units where there are steric difficulties in self-termination. The probability of self-termination for larger diradicals is so great that the high polymer obtained in thermal polymerization must have been formed through an alternative monoradical process.

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DETERMINATION OF DIELECTRIC CONSTANT IN BINARY ORGANIC SYSTEMS¹

C. G. MILLER² AND O. MAASS

ABSTRACT

Measurements of the dielectric constants of binary systems have been made; hexane, benzene, toluene, acetone, isopropyl alcohol, and nitrobenzene have been used two at a time. It was the purpose to obtain accurate data for the dielectric constants for the 15 systems over the whole range of concentrations from 0 to 100%, with the absolute accuracy of 0.1%. It is claimed that the relative accuracy is of this order. From the data obtained regularities have been found which are expressed in the form of empirical equations which summarize the data. Tentative suggestions regarding theoretical conclusions are made in a number of cases.

INTRODUCTION

There are already extensive data in the literature concerning the dielectric constants of binary organic mixtures (1). These data have been obtained over a period of years by a number of investigators and by a number of different techniques. While some of the systems investigated in the present work have been recorded elsewhere, in most cases these studies are isolated in the sense of dealing with a single system and in some cases only a relatively small concentration range has been considered within a given system. In addition the data are reported at various temperatures.

The initial objective of the authors was to build up a body of self-consistent dielectric constant data at a single temperature in those mixtures which would cover a wide range of dielectric constant, and over the complete range of concentration in a given system, with a view to investigating subsequently electrolytic conductivity in such mixtures.

In the furtherance of this objective, measurements were made of the dielectric constant in two-component systems which may be of interest per se. The 15 systems reported comprise a systematic study of mixtures of six compounds taken in pairs and cover a range of dielectric constant (ϵ) from 2 to 35. In this presentation it is considered an advantage for comparative purposes that all systems have been studied with the same apparatus and technique.

While the authors are interested in establishing the accuracy of the absolute values of their results, it may be pointed out that whatever error there may be in the measurements will be relative and will not affect the general nature of the conclusions drawn.

Those inferences drawn from the dielectric constant data in regard to certain regularities were so interesting that it was considered useful to record these regularities, although at this stage the authors do not contemplate making any theoretical deductions.

To assist in interpreting the results of the dielectric constant measurements, the densities of the various mixtures were required and were determined experimentally where adequate data were not readily available in the literature.

The technique of the measurement of dielectric constant follows fairly closely that of other investigators and whatever changes have been made are recorded in the experimental section.

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²National Research Council Postdoctorate Fellow 1957-58.

EXPERIMENTAL

A. Materials

Benzene and toluene (Mallinckrodt "Analytical Reagent"), normal hexane and cyclohexane (Phillips "Pure Grade") were all used without further purification. The dielectric constant was taken as the criterion of purity and its values for all the hydrocarbons agreed closely with the accepted values for the pure liquids.

Acetone (Mallinckrodt "Analytical Reagent") was dried by distillation from a large quantity of Drierite and allowed to stand over a small quantity of Drierite from which it was decanted for use.

Isopropanol (Eastman) was dried over freshly calcined lime and distilled from the lime immediately prior to each series of measurements.

Nitrobenzene (Eastman) was twice distilled in vacuum (less than 2 mm of mercury) and the distillate stored in a sealed container until used.

B. Apparatus and Procedure

The dielectric cell was of similar design and dimensions to that described by Gross and Taylor (2). The capacitor comprised two coaxial metallic cylinders, the medium under study filling the annular space between the cylinders. The outer cylinder was surrounded by a guard element which formed the body of the cell. These three elements were made from rhodium-plated brass. The assembly was held rigidly by teflon spacers and by a stainless steel lid which screwed down tightly and formed a part of the guard element. When assembled, the cell had an air capacitance of approximately $4.89 \mu\text{mf}$ and an internal volume of about 14 ml. The cell assembly was lowered into a grounded aluminum canister from which it was insulated electrically by a teflon ring, and the canister was immersed in a water thermostat maintained at $25^\circ \pm 0.01^\circ \text{C}$. The cell, once assembled and calibrated, was used for all measurements without disassembly.

Capacitance measurements were made by substitution on a capacitance bridge (General Radio type 716-C with guard circuit type 716-P4 and detector type 1231-BRF). Experiments on air and cyclohexane showed no variation in capacitance reading over the frequency range 1 kc/sec to 100 kc/sec. Accordingly the frequencies 1 kc/sec, 10 kc/sec, and 100 kc/sec were used indiscriminately throughout this work, the higher frequencies being preferred in the polar liquids where the dissipation factor was appreciable. All capacitance measurements were made by a reiterative method, sufficient readings being taken that the estimated probable error in the mean did not exceed 0.1% of the mean.

TABLE I
Cell capacitance using toluene

	C_i	B_0	Δ_{corr}	C_0	$C_0 - C_i$
1	100.18	111.90	+0.02	111.92	11.74
2	199.96	211.70	-0.02	211.69	11.73
3	400.24	412.04	-0.01	412.03	11.79
4	599.58	611.34	+0.01	611.35	11.77
5	800.24	812.06	-0.02	812.04	11.80
6	1000.12	1011.90	+0.01	1011.91	11.79
Mean					11.770 ± 0.012

By way of illustration, in Table I is given the record of an actual experiment using toluene as the dielectric. In operation the variable capacitor of the capacitance bridge was set to an arbitrary value with the cell in parallel with it. The bridge was balanced, the

cell removed from the circuit, and the bridge rebalanced by means of increasing the capacitance of the variable capacitor. The difference in reading gives the capacitance of the cell. In Table I, C_1 is the reading of the variable capacitor with the cell in the circuit, B_0 the reading of the variable capacitor when the cell has been removed, Δ_{corr} the net correction as obtained from the bridge calibration and applied to B_0 , C_0 the corrected value for B_0 (that is, $C_0 = B_0 + \Delta_{\text{corr}}$), and finally $C_0 - C_1$ represents the capacitance of the cell.

The probable error in the mean, ± 0.012 , was estimated from the expression: $R = \pm 0.6745 \sqrt{\{\sum V^2/n(n-1)\}}$ where R is the probable error, V the individual deviations from the mean, and n the number of readings taken.

A correction for switch and lead capacitance was made by the same reiterative method and was applied to capacitance readings as follows:

Observed capacitance	$11.770 \pm 0.012 \mu\text{f}$
Switch correction	$-0.157_5 \pm 0.001_4 \mu\text{f}$
Net cell capacitance	$11.612 \pm 0.013 \mu\text{f}$
Cell constant (previously determined)	$4.887 \pm .005 \mu\text{f}$
Dielectric constant of toluene	$\frac{11.612}{4.887} = 2.376 \pm 0.005$

The dielectric cell was calibrated with air as the dielectric and cyclohexane was used as a secondary standard, as recommended by Hartshorn and his co-workers (3). Excellent agreement (0.1%) was obtained, and the true cell constant was taken as the mean, with the value obtained from cyclohexane given half-weight.

Density measurements were performed with a Westphal balance. The temperature of the liquid was measured to 0.2°C and the density corrected to 25.0°C , assuming the temperature coefficients of the pure liquids to persist in the mixtures.

All mixtures were prepared by volume, the temperature of the pure liquids being measured and the molar percentages calculated from the density data given by Timmermans (4).

RESULTS

A comparison between observed values of dielectric constant for the pure liquids (ϵ_{obs}) and the accepted values (ϵ_{ref}) as recorded by Maryott and Smith (5) is given in Table II. All the observed values are thought to be accurate to $\pm 0.2\%$ except that for

TABLE II
Dielectric constants of pure liquids at 25°C

Compound	ϵ_{obs}	ϵ_{ref}
n-Hexane	1.884 ± 0.004	1.882 ± 0.01
Benzene	2.281 ± 0.006	2.274 ± 0.002
Toluene	2.376 ± 0.005	2.379 ± 0.01
Isopropanol	19.13 ± 0.04	18.3 ± 0.4
Acetone	20.54 ± 0.04	$20.7_0 \pm 0.4$
Nitrobenzene	34.62 ± 0.07	34.82 ± 0.07

benzene, which is slightly high, due probably to a small amount of moisture in the sample. Hartshorn (3) has shown that traces of water in benzene cause a high dielectric constant and are extremely difficult to remove. No attempt was made to dry the benzene used in this work.

There is a notable discrepancy between the observed dielectric constant of isopropanol and that recorded by Maryott and Smith. However, these authors, when selecting the value 18.3 as the dielectric constant of isopropanol, neglected the value 20.1 recorded by Hennings (6) although they suggested that Hennings' value be considered in any future revision of the data. Since the interest in the present work lay largely in the relative variation of dielectric constant with composition, no attempt was made to resolve this discrepancy. All dielectric constant values, whether for mixtures or for pure liquids, are internally consistent to $\pm 0.1\%$.

In Table III (A, B, and C) are recorded the experimental determinations of the dielectric constants for the various mixtures. For each system the mole fraction refers to

TABLE IIIA
Dielectric constants of hydrocarbon systems
(experimental values)

Toluene in benzene		Benzene in hexane		Toluene in hexane	
Mol. Fr.	ϵ	Mol. Fr.	ϵ	Mol. Fr.	ϵ
0	2.281	0	1.884	0	1.884
0.173	2.290	0.269	1.945	0.235	1.967
0.358	2.312	0.495	2.024	0.451	2.063
0.556	2.329	0.688	2.102	0.648	2.161
0.770	2.350	0.855	2.186	0.831	2.266
1.00	2.376	1.00	2.281	1.00	2.376

TABLE IIIB
Dielectric constants of non-hydroxylic systems
(experimental values)

Acetone in hexane		Acetone in benzene		Acetone in toluene		Nitrobenzene in hexane	
Mol. Fr.	ϵ	Mol. Fr.	ϵ	Mol. Fr.	ϵ	Mol. Fr.	ϵ
0	1.88 ₄	0	2.28 ₁	0	2.37 ₆	0	1.88 ₄
0.308	4.40 ₀	0.232	4.99 ₇	0.265	4.98 ₅	0.242	6.17 ₁
0.542	7.69 ₆	0.446	8.12 ₂	0.490	8.19 ₇	0.460	11.92
0.727	11.68	0.644	11.85	0.742	13.24	0.657	19.04
0.876	16.01	0.828	15.97	0.852	16.07	0.836	26.65
1.00	20.54	1.00	20.54	1.00	20.54	1.00	34.62

Nitrobenzene in benzene		Nitrobenzene in toluene		Nitrobenzene in acetone	
Mol. Fr.	ϵ	Mol. Fr.	ϵ	Mol. Fr.	ϵ
0	2.28 ₁	0	2.37 ₆	0	20.54
0.178	6.58 ₃	0.206	6.72 ₀	0.152	23.36
0.367	11.90	0.409	11.99	0.324	26.00
0.566	18.26	0.609	18.45	0.519	28.75
0.776	25.65	0.806	25.81	0.742	31.46
1.00	34.62	1.00	34.62	1.00	34.62

TABLE IIIC
Dielectric constants of hydroxylic systems
(experimental values)

Isopropanol in hexane		Isopropanol in benzene		Isopropanol in toluene	
Mol. Fr.	ϵ	Mol. Fr.	ϵ	Mol. Fr.	ϵ
0	1.88 ₁	0	2.28 ₁	0	2.37 ₁
0.300	2.78 ₅	0.226	3.44 ₀	0.258	3.52 ₃
0.533	5.88 ₇	0.437	6.04 ₁	0.482	6.21 ₂
0.720	10.27	0.636	9.89 ₄	0.776	10.12
0.873	14.96	0.824	14.57	0.848	14.68
1.00	19.13	1.00	19.13	1.00	19.13

Nitrobenzene in isopropanol		Acetone in isopropanol	
Mol. Fr.	ϵ	Mol. Fr.	ϵ
0	19.13	0	19.13
0.158	20.08	0.207	17.62
0.333	21.98	0.410	17.34
0.529	24.91	0.610	17.95
0.749	28.93	0.806	19.26
1.00	34.62	1.00	20.54

the first named component and it is the more polar. Measured dielectric constants are plotted for selected systems in Fig. 1 (*a, b, c*). The curve for the nitrobenzene-acetone system is slightly convex upward; the system acetone-isopropanol exhibits a minimum in dielectric constant at about 0.35 mole fraction acetone; the system toluene-benzene shows a linear variation in dielectric constant with composition; all other systems studied show a downward convexity in the dielectric constant-composition curve. Typical examples of this latter behavior are shown in Fig. 1*a* for nitrobenzene-hexane and in Fig. 1*c* for the benzene-hexane and toluene-hexane systems.

Table IV (parts 1, 2, 3) contains the values of density (column 2) and dielectric constant (column 3) at the selected concentrations (column 1) of 0, 0.20, 0.40, 0.60, 0.80, and 1.00 mole fraction. As in Table III the mole fraction refers to the first-named component of each system. Experimental values of dielectric constant and density relative to molecular concentration were plotted on graphs from which the values at the selected concentrations were read. The error in the values thus derived can be expected to be at least as small as the error in any specific measurement.

Where density data for the mixtures were readily available no measurements were made. The density values taken from the literature were corrected by a constant amount over the whole concentration range in a given system in order to bring the densities of the pure liquids to the values given by Timmermans (4) and accepted in the remainder of this work. In only one system (acetone-benzene) was this correction of a significant magnitude, and amounted to about 0.2%. The systems so corrected were acetone-benzene (correction -0.0016) (7); nitrobenzene-benzene (correction 0.004) (7); and acetone-isopropanol (correction 0.0005) (8). Rakshit (9) has shown that density is a linear function of composition in the toluene-benzene system at 20° C. The densities for this system in Table IV have been calculated on the assumption of a similar linearity at 25° C.

For the remaining 11 systems the densities were determined experimentally as described

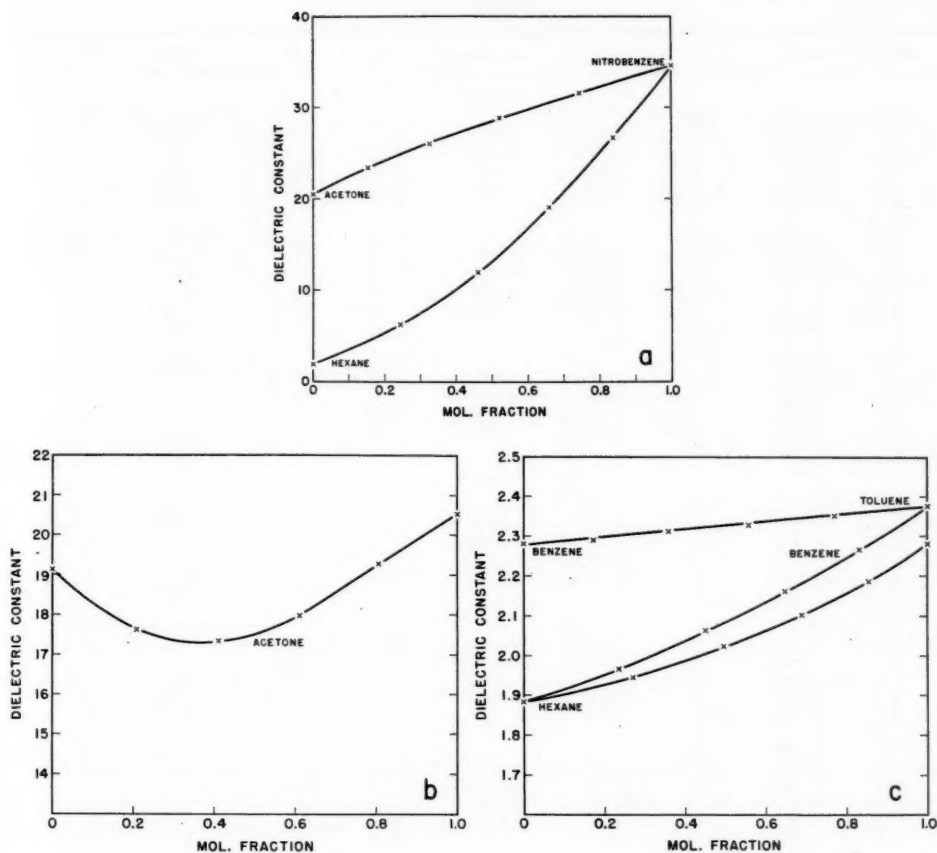


FIG. 1. (a) Measured dielectric constants in two nitrobenzene systems.
 (b) Measured dielectric constants in acetone-isopropanol system.
 (c) Measured dielectric constants in three hydrocarbon systems.

above. The temperature correction was small in all determinations and the accuracy of the density data is estimated at $\pm 0.1\%$ absolute.

In addition to the columns relating to molecular concentration, density, and dielectric constant, Table IV contains several columns which will be described fully in the discussion but which may be mentioned briefly here. The fourth column shows calculated values of dielectric constant based on a relationship which will be dealt with later, and the difference between this value and the observed is given in the fifth column. The next two columns contain calculated values of the so-called molecular polarizations of the mixture and of the relatively more polar component respectively. Finally, the values of K_1 and K_2 from the empirical relationship to be discussed below, together with a qualitative indication of the relative variation of the dielectric constant and of the density over the whole range of concentration are shown in column eight.

TABLE IV

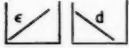
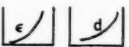
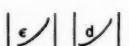
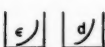
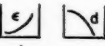
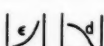
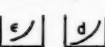
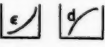
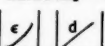
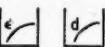










Mol. Fr.	Density	ϵ_{obs}	ϵ_{calc}	$\epsilon_{\text{obs}} - \epsilon_{\text{calc}}$	P_{12}	P_2	
Part 1							
0.0	0.874	2.281			26.8		Toluene in benzene $K_1 = 8.337$ $K_2 = 0$
0.2	0.871	2.298	2.298	0.0	28.0	33.2	
0.4	0.869	2.319	2.319	0.0	29.4	33.4	
0.6	0.867	2.338	2.338	0.0	30.8	33.4	
0.8	0.864	2.357	2.357	0.0	32.1	33.5	
1.0	0.862	2.376			33.6	33.6	
0.0	0.655	1.884			29.9		Benzene in hexane $K_1 = 1.451$ $K_2 = 1.665$
0.2	0.686	1.928	1.930	-0.002	29.0	25.4	
0.4	0.722	1.987	1.989	-0.002	28.4	26.2	
0.6	0.763	2.060	2.060	± 0.000	27.8	26.4	
0.8	0.813	2.154	2.153	+0.001	27.2	26.6	
1.0	0.874	2.281			26.8	26.8	
0.0	0.655	1.884			29.9		Toluene in hexane $K_1 = 1.967$ $K_2 = 1.964$
2.0	0.691	1.955	1.956	-0.001	30.6	33.0	
4.0	0.728	2.034	2.034	± 0.000	31.2	33.0	
6.0	0.768	2.135	2.133	+0.002	32.1	33.5	
8.0	0.813	2.247	2.244	+0.003	32.8	33.6	
1.0	0.862	2.376			33.6	33.6	
Part 2							
0.0	0.655	1.88			29.9		Acetone in hexane $K_1 = 115.3$ $K_2 = 214.8$
0.2	0.667	3.39	3.33	+0.06	53.5	147.9	
0.4	0.684	5.38	5.41	-0.03	65.0	107.6	
0.6	0.708	8.78	8.57	+0.21	70.7	97.8	
0.8	0.739	13.60	13.36	+0.24	69.6	79.5	
1.0	0.785	20.54			64.1	64.1	
0.0	0.874	2.28			26.8		Acetone in benzene $K_1 = 132.2$ $K_2 = 831.5$
0.2	0.859	4.57	4.41	+0.16	46.9	127.4	
0.4	0.842	7.35	7.34	+0.01	58.0	105.0	
0.6	0.824	10.87	10.90	-0.03	61.5	84.7	
0.8	0.805	15.31	15.17	+0.14	63.1	73.0	
1.0	0.785	20.54			64.1	64.1	
0.0	0.862	2.38			33.6		Acetone in toluene $K_1 = -171.4$ $K_2 = 829.0$
0.2	0.852	4.26	4.23	+0.03	51.9	125.0	
0.4	0.839	6.73	6.75	-0.02	61.4	108.1	
0.6	0.824	10.14	10.10	+0.04	64.5	86.8	
0.8	0.806	14.63	14.76	-0.13	66.0	74.1	
1.0	0.785	20.54			64.1	64.1	
0.0	0.655	1.88			29.9		Nitrobenzene in hexane $K_1 = 32.49$ $K_2 = 51.09$
0.2	0.747	5.30	5.27	+0.03	73.8	249.1	
0.4	0.849	10.21	10.16	+0.05	89.7	179.3	
0.6	0.961	16.74	16.55	+0.19	94.7	137.9	
0.8	1.076	24.96	24.55	+0.41	95.6	112.0	
1.0	1.148	34.62			94.3	94.3	
0.0	0.874	2.28			26.8		Nitrobenzene in benzene $K_1 = 54.33$ $K_2 = 165.3$
0.2	0.948	7.16	7.10	+0.06	61.8	202.6	
0.4	1.016	12.80	12.97	-0.17	75.4	148.4	
0.6	1.080	19.39	19.44	-0.05	83.7	121.6	
0.8	1.140	26.46	26.13	+0.33	89.6	105.2	
1.0	1.198	34.62			94.3	94.3	
0.0	0.862	2.38			33.69		Nitrobenzene in toluene $K_1 = 53.53$ $K_2 = 126.8$
0.2	0.929	6.44	6.53	-0.09	67.9	205.0	
0.4	0.996	11.78	11.72	-0.04	82.1	154.8	
0.6	1.064	18.19	18.26	-0.07	88.6	125.3	
0.8	1.130	25.60	25.82	-0.20	92.2	106.9	
1.0	1.198	34.62			94.3	94.3	
0.0	0.785	20.54			64.1		Nitrobenzene in acetone $K_1 = 31.63$ $K_2 = 5.829$
0.2	0.987	24.15	24.14	+0.01	70.1		
0.4	0.992	27.18	27.20	-0.02	76.1		
0.6	1.052	29.81	29.75	-0.06	83.6		
0.8	1.138	32.28	32.16	-0.12	88.3		
1.0	1.198	34.62			94.3		

TABLE IV (concluded)

Mol. Fr.	Density	ϵ_{obs}	ϵ_{calc}	$\epsilon_{\text{obs}} - \epsilon_{\text{calc}}$	P_{12}	P_2	
Part 3							
0.0	0.655	1.88			29.9		Isopropyl alcohol in
0.2	0.668	2.28	2.67	-0.39	36.2	61.5	hexane
0.4	0.686	3.83	4.16	-0.33	53.6	89.0	$K_1 = 54.41$ $K_2 = 48.48$
0.6	0.711	7.37	7.32	+0.05	67.4	92.4	 
0.8	0.742	12.68	11.45	+1.23	70.0	80.1	
1.0	0.781	19.13			66.0	66.0	
0.0	0.874	2.28			26.8		Isopropyl alcohol in
0.2	0.856	3.27	3.49	-0.22	37.5	80.5	benzene
0.4	0.837	5.40	5.61	-0.21	50.3	85.7	$K_1 = 38.3$ $K_2 = 1545.0$
0.6	0.819	9.17	9.03	+0.14	60.1	82.3	 
0.8	0.801	14.96	14.00	+0.95	65.4	74.9	
1.0	0.781	19.13			66.0	66.0	
0.0	0.862	2.38			33.6		Isopropyl alcohol in
0.2	0.848	3.11	3.46	-0.29	41.5	73.0	toluene
0.4	0.834	4.98	5.24	-0.26	54.2	85.1	$K_1 = 48.48$ $K_2 = 1938.0$
0.6	0.820	8.46	8.09	+0.37	63.5	83.4	 
0.8	0.802	13.33	12.31	+1.02	66.7	75.0	
1.0	0.781	19.13			66.0	66.0	
0.0	0.781	19.13			66.0		Nitrobenzene in
0.2	0.890	20.50	20.38	+0.12	70.8		isopropyl alcohol
0.4	0.982	22.89	22.75	+0.14	76.4		$K_1 = 0.24$ $K_2 = 21.76$
0.6	1.064	25.08	26.28	-0.20	81.8		 
0.8	1.135	29.41	30.20	-0.75	88.1		
1.0	1.198	34.62			94.3		
0.0	0.781	19.13			66.0		Acetone in isopropyl
0.2	0.780	17.65	17.56	+0.09	64.1		alcohol
0.4	0.780	17.28	17.17	+0.11	64.2		$K_1 = 1345$ $K_2 = 2.444 \times 10^8$
0.6	0.780	17.98	18.40	-0.42	64.1		 
0.8	0.782	19.28	20.29	-1.01	64.2		
1.0	0.785	20.54			64.1		

Also to be described in detail later is Fig. 2 in which are plotted the molecular polarization of the mixture and the molecular polarization of the more polar component as these are tabulated in columns 6 and 7, Table IV.

DISCUSSION

The application of the theory of dielectric constants of binary systems to the interpretation of experimental data has not been very fruitful. At best it can be said that theory has indicated certain trends which have been borne out. This is so, for instance, in regard to molecular polarization, which will be referred to later.

That density and dielectric constant of a medium are related has been indicated, at least in so far as pure compounds are concerned. In a two-component system certain relationships between dielectric constant and density have been suggested. Having this in mind, the relationship of dielectric constant with density which was observed was found to lend itself to algebraic expression within certain limits for a number of systems including those having a polar compound as one of the components.

In the following discussion ϵ_1 and ϵ_2 are the dielectric constants of the pure components of a binary mixture in which $\epsilon_2 > \epsilon_1$. The corresponding densities are d_1 and d_2 ; ϵ_{12} and d_{12} are dielectric constant and density respectively of the mixture. The first approach is that

$$[1] \quad \epsilon_{12} = \epsilon_1 + K(d_{12} - d_1).$$

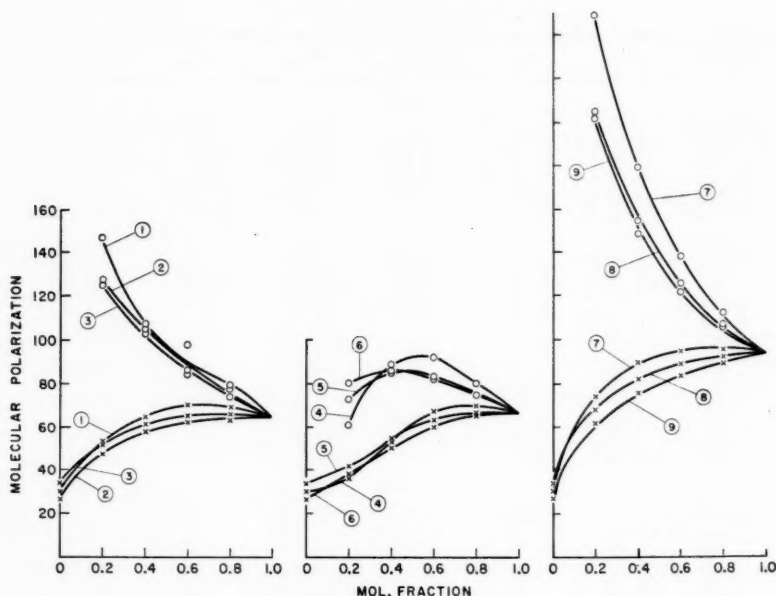


FIG. 2. Calculated values of molecular polarization.
 $\times = P_{12}$, $\circ = P_2$. (1) Acetone-hexane. (2) Acetone-benzene. (3) Acetone-toluene. (4) Isopropanol-hexane. (5) Isopropanol-toluene. (6) Isopropanol-benzene. (7) Nitrobenzene-hexane. (8) Nitrobenzene-toluene. (9) Nitrobenzene-benzene.

This is in agreement within experimental error only in the system benzene-toluene. Even with the hexane-benzene and hexane-toluene systems this does not hold. However, if instead of the above simple relationship we use

$$[2] \quad \epsilon_{12} = \epsilon_1 + K_1(d_{12} - d_1) + K_2(d_{12} - d_1)^2,$$

there is perfect agreement in the hydrocarbon systems between the calculated and observed results (Table IV, part 1).

Having found this perfect agreement between the empirical relationship (2) and the experimental results in a limited number of systems, an examination of the application of this to all the other systems examined was made.

From the qualitative graphical representation of the relation between dielectric constant and composition, and density and composition, respectively, made in the final column of Table IV it is obvious that the relative convex and concave curvature, as between dielectric constant and composition on the one hand and density and composition on the other, varies from system to system, and it might seem that no particular regularity could be expected. Nevertheless, when equation [2] is applied, this relationship is found to be in fairly good agreement with the experimental results as far as systems involving only one polar compound are concerned (Table IV, part 2) and even indicatively correct for systems involving two so-called polar compounds.

Calculations show that in the hydrocarbon systems (Table IV, part 1) equation [2] hold exactly. In Table IV (part 2) the average difference between observed and calculated values is 0.9% and in Table IV (part 3) 4.0%.

Reference to column 7, in Table IV, part 1, shows that the molecular polarization remains essentially constant with dilution for the hydrocarbons used in this work. This constancy can be made use of in the calculation of P_2 , the molecular polarization of the more polar component.

Figure 2 contains three families of curves representing systems containing acetone, isopropanol, and nitrobenzene respectively. For each polar compound the three curves represent mixtures with the hydrocarbons taken in turn. These curves are plots of the calculated values of P_{12} and P_2 as given in Table IV (parts 2 and 3). There is an essential similarity for curves for all hydrocarbons. In benzene and toluene they are almost contiguous while an appreciable divergence is noted for hexane.

A difference in shape is noted in the P_2 curve for systems containing acetone and nitrobenzene as distinct from the systems containing isopropanol. The increase in molecular polarization of acetone and nitrobenzene with increasing dilution may be explained simply by postulating an association between the dipoles in concentrated solution, an association that results in a partial cancellation of the moments of the associated dipoles. As the dilution increases fewer of the molecules exist in the associated state and each exerts its own moment.

The behavior of isopropanol in giving maxima in the P_2 curves calculated for systems containing hydrocarbons is common to other alcohols as well (10). An explanation which has been advanced for this behavior in the past supposes that two different mechanisms of association exist in binary mixtures of alcohols and hydrocarbons. The first mechanism is similar to that advanced above and accounts for the portion of the P_2 curve to the right of the maximum. As the concentration of alcohol is still further reduced, however, the dominant form of association is one in which the alcohol molecules are lined up, perhaps in chains, in such a way that the moments reinforce each other. As this type of association is reduced with increasing dilution the effective moment of each molecule and hence the apparent molecular polarization is also reduced.

CONCLUSION

It has been shown that the dielectric constants of binary systems are dependent on their density and the polarity of each of the components. Certain regularities have been established by summarizing the results obtained in the form of empirical equations. Aberrations from these equations can in the main be attributed to so-called association of one of the components, an association that is affected by the concentration of the second component.

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THE POLYSACCHARIDES OF *CRYPTOCOCCUS LAURENTII* (NRRL Y-1401)

PART I¹

M. J. ABERCROMBIE, J. K. N. JONES, M. V. LOCK,² M. B. PERRY, AND R. J. STOODLEY

ABSTRACT

The extracellular polysaccharides produced by *Cryptococcus laurentii* have been isolated and shown to consist of (A) an acidic polysaccharide containing D-mannose, D-xylose, and D-glucuronic acid; (B) a neutral polysaccharide containing D-glucose only.

Preliminary structural studies on the acidic material suggest that it consists of a mannose-containing backbone with xylose and glucuronic acid as end groups, while the glucan contains 1 → 3, 1 → 4, 1 → 2, and (or) 1 → 6 linked residues.

INTRODUCTION

Much is known about the origin of sugars found in homopolysaccharides (1-11). On the other hand the origin of sugars in heteropolysaccharides has not been investigated to any great extent (12, 13).

As part of a program for investigating the biosynthesis of monosaccharides found in heteropolysaccharides, we have studied the extracellular polysaccharide produced by the yeast organism *Cryptococcus laurentii*.

This organism, kindly supplied by the United States Department of Agriculture, Peoria, Illinois, was chosen because it produced high yields of polysaccharides from a wide variety of sugar substances.

Cryptococcus laurentii was grown on an unbuffered casamino acids-salts medium with glucose as the main carbon source (14). An acidic and a neutral polysaccharide were isolated by the following procedure, which was considered unlikely to cause degradation of the polysaccharides. The cell-free solution was dialyzed and then passed through an ion exchange column to give a clear, light brown viscous solution. After the solution was concentrated, the polysaccharides were precipitated with ethanol and had $[\alpha]_D +27^\circ$. Chromatographic examination of the acid hydrolyzate showed sugars which moved at rates corresponding to mannose, xylose, glucuronic acid, and glucose. The sugars were obtained crystalline or as crystalline derivatives and were shown to be D-mannose, D-xylose, D-glucose, and D-glucuronic acid. The crude polysaccharide showed two peaks on electrophoresis in a veronal buffer. On addition of an aqueous solution of 'cetavlon' (cetyltrimethyl-ammonium bromide) to an aqueous solution of the polysaccharide an insoluble cetyltrimethyl-ammonium salt of an acidic polysaccharide was precipitated. This salt was dissolved in 10% aqueous sodium chloride solution and the sodium salt of the acidic polysaccharide was precipitated in ethanol. Chromatographic examination of the acid hydrolyzate of this material showed mannose, xylose, and glucuronic acid to be present. Electrophoresis in veronal and borate buffers showed a single peak: glass paper electrophoresis (17) showed a single spot. Further attempts at fractionation failed to give any separation. The supernatant from the cetyltrimethyl-ammonium precipitate was concentrated and added to ethanol. Mainly glucose and traces of mannose, xylose, and glucuronic acid were detected in the precipitated material (chromatography).

The acidic polysaccharide had $[\alpha]_D +21^\circ$; the molar ratio of mannose to xylose present

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Contribution from the Department of Chemistry, Queen's University, Kingston, Ontario, Canada.

²On leave of absence from British Rayon Research Association, Heald Green Laboratories, Wythenshawe, Manchester 22, England.

in this material was found to be 5:2 (18); titration of the polysaccharide with standard sodium hydroxide gave a uronic acid content of 14.4%. Determination of uronic acid content by the carbazole method (19) gave 11.8%.

On oxidation with sodium metaperiodate the acid polysaccharide consumed 1.10 moles of sodium metaperiodate and liberated 0.58 mole of formic acid per sugar residue. These figures appear to indicate that end group or 1 \rightarrow 6 linked hexose only is oxidized since a sugar which contains hydroxyl groups on each of three contiguous carbon atoms will reduce 2 moles of periodate and yield 1 mole of formic acid per mole. However, glucuronic acid is present as an end group which is known to overoxidize easily. Hence no exact interpretation can be placed on these results. The oxidized material was reduced with sodium borohydride and hydrolyzed: chromatographic examination of the hydrolyzate showed mannose to be the only sugar present.

Hydrolysis of the acidic polysaccharide in the presence of Amberlite 1R-120 (H) resin removed considerable quantities of xylose without liberating mannose or glucuronic acid. This treatment was repeated with fresh resin until no more xylose was liberated. Chromatographic examination of the hydrolyzate of the resin resistant polysaccharide showed mannose, glucuronic acid, and some xylose. The mannose to xylose molar ratio (18) was determined and found to be 25:3; thus about 66% of the xylose had been hydrolyzed.

The results obtained from sodium metaperiodate oxidation and resin hydrolysis suggest that the polysaccharide consists of a resistant mannose containing backbone with xylose and glucuronic acid as end groups.

The glucan had $[\alpha]_D +180^\circ$ but was contaminated with traces of the acidic polysaccharide. It did not give a blue color with iodine nor was it hydrolyzed by β -amylase.

On oxidation with sodium metaperiodate the polysaccharide consumed 0.83 ± 0.07 mole of metaperiodate and liberated 0.14 ± 0.04 mole of formic acid per anhydro hexose unit. These results indicate that about 1 glucose residue in 10 contains hydroxyl groups in each of three contiguous carbon atoms and that about 40% of the glucose residues do not contain adjacent hydroxyl groups. The oxidized material was reduced with sodium borohydride and hydrolyzed. Chromatographic examination of the hydrolyzate showed glucose, erythritol, and glycerol to be present, suggesting the presence of 1 \rightarrow 3, 1 \rightarrow 4, 1 \rightarrow 2, and (or) 1 \rightarrow 6 linked residues.

EXPERIMENTAL

The following solvent systems (v/v) were used to separate sugars on paper chromatograms: (A) butanol:pyridine:benzene:water, 5:3:3:1; (B) ethyl acetate:acetic acid:water, 9:2:2; (C) butanol:ethanol:water, 3:1:1. Sugars were detected on paper chromatograms by spraying the chromatograms with either *p*-anisidine hydrochloride (20) or alkaline silver nitrate (21). Solutions were evaporated under reduced pressure at ca. 40°C. All optical rotations were measured in aqueous solution at $23^\circ \pm 3^\circ$ C unless otherwise stated.

Growth of Cryptococcus laurentii and Isolation of the Polysaccharide

The following two media were prepared and each was electrometrically adjusted to pH 7.0 with dilute potassium hydroxide solution: (i) 'Difco' bactocasamino acids (15 g), potassium nitrate (5 g), potassium dihydrogen phosphate (20 g), dipotassium hydrogen phosphate (15 g), magnesium sulphate heptahydrate (2.5 g), thiamine hydrochloride (5 mg), trace element solution (25 ml) (15), water (4l); (ii) glucose (250 g), water (1 liter). The trace element solution contained zinc sulphate heptahydrate (2.0 g), copper

sulphate pentahydrate (0.1 g), manganese sulphate monohydrate (1.5 g), ferrous sulphate heptahydrate (2.0 g), and distilled water (1 liter).

Medium (i) was equally distributed between 10 conical flasks (1 liter), the necks of which were plugged with cotton wool. Both media were steam-sterilized for 15 minutes at a pressure of 15 p.s.i. Aliquots (ca. 100 ml) of the glucose solution were added to each flask under sterile conditions and the solutions were inoculated with an aqueous suspension of *Cryptococcus laurentii*. The flasks were swirled on a mechanical shaker at $20^{\circ} \pm 2^{\circ}$ C for 14 days, after which the culture medium had become extremely viscous.

The combined solution was diluted with water (2 vol.) and centrifuged on a Sharples ultracentrifuge to remove suspended yeast cells. The supernatant was dialyzed against tap water (3 days) and distilled water (1 day). The clear, light brown solution was passed through an Amberlite IR-120 (H) resin column: since the solution was slightly cloudy it was again centrifuged on the Sharples ultracentrifuge. The solution was concentrated on a continuous evaporator at 35° C until a highly viscous solution was obtained. This solution was poured into ice-cold ethanol (6 vol. containing 1% hydrochloric acid) with vigorous stirring. The fibrous white product, suspended in ethanol, was broken up in a Waring Blender: the finely divided material was washed with ethanol until free of chloride ions. This material was collected by filtration, dried *in vacuo* over calcium chloride, and had $[\alpha]_D +27^{\circ}$ (yield 19 g, 8% based on glucose).

Chromatographic examination of the polysaccharide hydrolyzate in solvents A and B indicated the presence of mannose, xylose, glucuronic acid, and glucose.

Neutral Component Sugars of the Polysaccharide

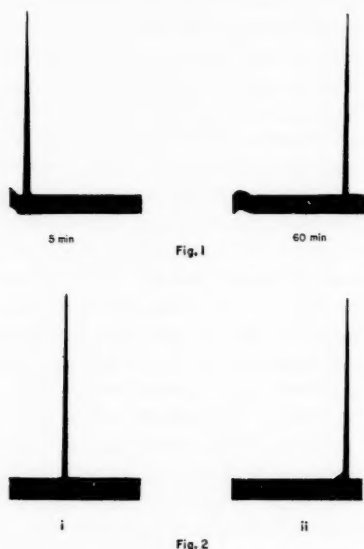
The polysaccharide (500 mg) was heated with *N* sulphuric acid (50 ml) for 24 hours on a boiling water bath. The solution was neutralized (BaCO_3), filtered, and deionized by passage through an Amberlite IR-120 (H) resin column. The solution was concentrated to a syrup and fractionated by paper chromatography using solvent A. Extraction of the appropriate sections of the paper afforded crystalline D-xylose, m.p. $142\text{--}143^{\circ}$, $[\alpha]_D +17.6^{\circ}$; D-glucose, m.p. 145° , $[\alpha]_D +50^{\circ}$, which gave a N-*p*-nitrophenyl- β -D-glucosylamine (22), m.p. 185° , $[\alpha]_D -200^{\circ}$ (pyridine); D-mannose (crystallized after seeding and standing 4 weeks), m.p. 133° C, $[\alpha]_D +13^{\circ}$, which gave D-mannose phenylhydrazone, m.p. $188\text{--}190^{\circ}$ C (mixture melting points with authentic samples showed no depression). The glucuronolactone failed to crystallize. A spot of the D-glucose solution gave a positive test when sprayed with the glucose oxidase reagent (23).

Free Electrophoresis of the Polysaccharide

The polysaccharide in solution at a concentration of 1.0% in veronal buffer (0.1 *M* barbital/sodium hydroxide pH 9.5) was subjected to electrophoresis in a Perkin-Elmer Model 38-A moving boundary apparatus (1° C). The polysaccharide solution was dialyzed against the veronal buffer for 48 hours to gain full equilibration of the ionic concentrations prior to electrophoresis. Figure 1 is the diagram obtained in the descending arm after 5 and 60 minutes. Two peaks were observed, a fast-moving peak and a stationary small peak. Electrophoresis was continued until the fast-moving peak had moved off the screen. Chromatographic examination of the hydrolyzate of the solutions contained in the solution, buffer, and middle arms of the electrophoresis cell showed that the fast-moving peak was an acidic polysaccharide containing mannose, xylose, and glucuronic acid. The stationary peak was a polysaccharide containing mainly glucose.

Fractionation of the Polysaccharide

The polysaccharide mixture was dissolved in water (5 liters): to this solution was



FIGS. 1 and 2. Free electrophoresis of polysaccharide.

added a 2.5% solution of 'cetavlon' with stirring until no further precipitate formed (15, 16). The white material was collected by centrifugation, washed well with water, and dissolved in 10% aqueous sodium chloride solution (500 ml). The solution was poured into ice-cold ethanol (6 vol.) and the precipitated polysaccharide was washed with 95% aqueous ethanol. The polysaccharide (sodium salt) was collected by filtration, dried *in vacuo* over calcium chloride, and had $[\alpha]_D +21^\circ$, ash 4.5%, and nitrogen content 0.1% (yield 17 g). Chromatographic examination of the hydrolyzate in solvents A and B indicated the presence of mannose, xylose, and glucuronic acid. The supernatant from the 'cetavlon' precipitate was dialyzed against tap water (4 days) and distilled water (1 day), concentrated, and poured into ice-cold ethanol. The small amount of white precipitate was collected by centrifugation, washed with ethanol, and dried (yield 1.0 g). Chromatographic examination of the hydrolyzate of this material indicated the presence of glucose and small quantities of mannose, xylose, and glucuronic acid.

Free Electrophoresis of the Acidic Polysaccharide

A 1% solution of the acidic polysaccharide in (i) borate buffer (0.05 M borate) and (ii) veronal buffer (as above) was subjected to electrophoresis. Figure 2 is the diagram obtained in the descending arm in each buffer: only a single peak was observed.

Glass Paper Electrophoresis

The glass paper electrophoresis was carried out as described by Smith and Lewis (17). A type 3371 B LKB power supply was used with 2 N sodium hydroxide as the electrolyte. The chromatogram was sprayed with sulphuric acid/*p*-anisidine. The electrophoresis was repeated ($\times 4$); in each case a single spot was observed.

Reduction of the Acidic Polysaccharide

The sodium salt of the acidic polysaccharide (100 mg, glucose-free) was dissolved in water (10 ml) and deionized by passing its solution through a small column of Amberlite IR-120 (H) resin. The solution was concentrated and lyophilized. The residual material was suspended in methanol and an ethereal solution of diazomethane was added with stirring until a permanent yellow color was obtained. The polysaccharide was collected by filtration, washed with methanol, and dissolved in water. An excess of sodium borohydride (50 mg) was added and the reaction was allowed to stand at room temperature for 5 hours. The excess sodium borohydride was destroyed by the addition of acetic acid: the solution was dialyzed against distilled water for 24 hours and then passed through an Amberlite IR-120 (H) resin column. The deionized solution was concentrated and the polysaccharide precipitated by pouring the solution into ice-cold ethanol. The polysaccharide was collected by centrifugation. A small portion of this (ca. 5 mg) was hydrolyzed with *N* sulphuric acid as previously described. Chromatographic examination of the hydrolyzate in solvent A indicated the presence of mannose, xylose, glucuronic acid, and glucose. When sprayed with the glucose oxidase spray (23), a spot of the hydrolyzate gave a positive reaction for glucose. The treatment with diazomethane and reduction with sodium borohydride was repeated twice until the chromatographic examination of the hydrolyzate showed that only a trace of glucuronic acid remained. The remainder of the polysaccharide (ca. 60 mg) was hydrolyzed with *N* sulphuric acid on a boiling water bath, neutralized (BaCO_3), filtered, and deionized by passage of the solution through an Amberlite IR-120 (H) resin column. The solution was concentrated to a syrup which was fractionated by chromatography on Whatman 3MM paper by the use of solvent A. The appropriate section of the paper containing glucose was eluted and the solution concentrated to a syrup. The syrup was dissolved in methanol (1 ml) containing a trace of hydrochloric acid and 10 mg of *p*-nitroaniline was added: the reaction mixture was heated on a boiling water bath for 10 minutes; on cooling yellow crystals appeared, m.p. 185°C (mixture melting point with authentic *N*-*p*-nitrophenyl- β -D-glucosylamine was not depressed).

Quantitative Estimation of the Component Sugars of the Acidic Polysaccharide

Samples of the polysaccharide (30–40 mg) were hydrolyzed in the usual way. The syrup obtained was fractionated by chromatography on Whatman 3MM paper by the use of solvent A. The appropriate sections of paper were eluted and the ratio of mannose to xylose was determined by the phenol – sulphuric acid method (18). The results indicated that mannose and xylose were present in the molar ratio 5:2.

The glucuronic anhydride content of the polysaccharide was determined by the carbazole method (19) and found to be 11.8%. The ash-free polysaccharide had an equivalent weight of 1215 (\equiv 14.4% glucuronic anhydride), found by electrometric titration with standard alkali.

Sodium Metaperiodate Oxidation of the Acidic Polysaccharide

Accurately weighed samples of the polysaccharide (ca. 50 mg) were oxidized with aqueous sodium metaperiodate solution using standard procedures. The periodate uptake was estimated by the method of Neumuller and Vasseur (24) and the formic acid liberation by Andrews *et al.* (26). The results are collected in Table I.

When the oxidation with sodium metaperiodate was complete, ethylene glycol (3 ml) was added and the solution was dialyzed against distilled water for 24 hours. Sodium

TABLE I
Sodium metaperiodate oxidation of the acidic
polysaccharide per anhydro residue

Time (hr)	HCOOH	IO ₄
4.5	0.14	0.31
12.5	0.26	0.62
24.0	0.37	0.82
37.0	0.50	0.99
61.0	0.58	1.10
85.0	0.58	1.10
105.0	0.58	1.10

borohydride was added (50 mg) and the solution was left overnight and then dialyzed. The concentrated non-dialyzable material was hydrolyzed with *N* sulphuric acid in a sealed tube in a boiling water bath. Examination of the neutralized (BaCO₃) hydrolyzate on paper chromatograms showed mannose to be the only original sugar present.

Degradation of the Acidic Polysaccharide with Resin

The polysaccharide (500 mg) was dissolved in water (100 ml) and Amberlite IR-120 (H) resin (5 ml) was added. The reaction mixture was heated on a boiling water bath; at intervals, samples (ca. 1 ml) were withdrawn and examined chromatographically. Only xylose was detected; after 20 hours no apparent further release of xylose took place. The resin was removed by filtration and the solution concentrated and added to ice-cold ethanol, the precipitated polysaccharide (300 mg) was collected by centrifugation. The hydrolyzate of a small portion of this material (ca. 10 mg) was examined chromatographically; some xylose as well as mannose and glucuronic acid was present. The treatment with resin was repeated twice; only traces of xylose were removed by fresh resin: the weight of the polysaccharide remained constant during the two hydrolyses. The molar ratio of mannose to xylose was determined by the phenol-sulphuric acid method and found to be 25:3. Thus the hydrolysis of the polysaccharide with the resin had removed ca. 66% of the xylose without liberating mannose or glucuronic acid.

Examination of the Glucan

The glucan had $[\alpha]_D +180^\circ$: it did not give a blue color with iodine nor was it hydrolyzed with β -amylase.

Sodium Metaperiodate Oxidation of the Glucan

The oxidation of the glucan was carried out as described for the acidic polysaccharide. The results are collected in Table II. Extrapolation of the overoxidation part of the

TABLE II
The sodium metaperiodate oxidation of the glucan
per anhydro hexose residue

Time (hr)	HCOOH	IO ₄
2.75	—	0.65
5.75	—	0.78
10.50	0.14	0.84
25.00	0.20	0.98
54.50	0.24	1.06

curve to zero time gave a value corresponding to a metaperiodate uptake of 0.83 ± 0.07 mole and a liberation of 0.14 ± 0.04 mole of formic acid per anhydro hexose unit.

Hydrolysis of the Oxidized Glucan

The polysaccharide (50 mg) was oxidized with sodium metaperiodate as described. After 100 hours, ethylene glycol (5 ml) was added to destroy the excess periodate. The polyaldehyde was then reduced by the addition of a large excess of sodium borohydride and the solution stirred for 2 hours. The solution was acidified with dilute acetic acid and dialyzed against distilled water. The dialyzate, after concentration to dryness, was dissolved in *N* sulphuric acid and hydrolyzed for 10 hours. Chromatographic examination of the hydrolyzate in solvents A, B, and C, using *p*-anisidine hydrochloride and alkaline silver nitrate sprays, detected spots corresponding to glucose, glycerol, and erythritol.

Growth of Cryptococcus laurentii at pH 5, 7, and 9 and Isolation of the Polysaccharides

Culture media were prepared as before and each was adjusted to pH 5, pH 7, or pH 9. The media were treated in a similar manner to those described previously; after 12 days' shaking the solutions had become extremely viscous. The clear solutions were collected and the acidic polysaccharide and the glucan were isolated as previously described. The weights of the polysaccharides isolated from each growth media are shown in Table III.

TABLE III
Growth of *Cryptococcus laurentii* at various pH's

Initial pH of growth media	Yield of crude polysaccharide	Acidic polysaccharide	Glucan
5	12.0 g	6.5 g	4.0 g
7	10.0 g	9.0 g	0.2 g
9	7.0 g	6.5 g	—

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INDOLYL-3-PYRUVIC ACID OXIME AS THE PRECURSOR OF INDOLYL-3-ACETONITRILE¹

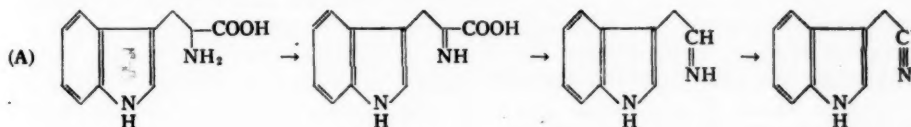
A. AHMAD AND IAN D. SPENSER

ABSTRACT

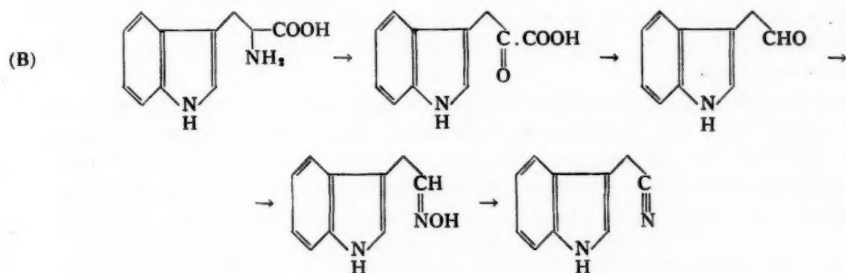
Chemical and chromatographic evidence is presented compatible with the hypothesis that the auxin indolyl-3-acetonitrile is derived in plants from indolyl-3-pyruvic acid oxime (anti HO- -COOH) by a concerted reaction.

Since the discovery that indolyl-3-acetonitrile (IAN) occurs naturally (1) and shows auxin activity in certain plant species, two hypotheses of its biosynthetic origin have been proposed. Both of these postulate tryptophan as the parent substance, but differ in the intermediate steps whereby the alanyl side chain of the amino acid is modified to -CH₂-CN in the nitrile.

Sequence A was the first to be put forward (1).



Experimental work (2) has established that IAN is indeed derived enzymatically from tryptophan in watermelon slices and in *Avena* coleoptiles. Incubation of the tissues with α -C¹⁴-tryptophan, followed by paper chromatographic analysis of extracts, gave rise to a number of radioactive spots, one of which was assigned to IAN. Another highly active spot was tentatively ascribed to indolyl-3-pyruvic acid, whose occurrence in plant extracts (3) had been the subject of controversy (4, 5, 6). A modified sequence of steps (sequence B) for IAN biosynthesis was suggested as a result of this tracer work (2).



Neither of the two hypotheses is entirely satisfactory. The first step of sequence A has many biochemical analogies, but amino acid oxidases, the type of enzyme required to catalyze such a reaction, are comparatively rare in plant tissues (7). The final step, dehydrogenation of an aldehyde imine to a nitrile, is without known chemical or biochemical precedent, and even the second step is unusual since in biochemical systems

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Contribution from the Department of Chemistry, McMaster University, Hamilton, Ontario.

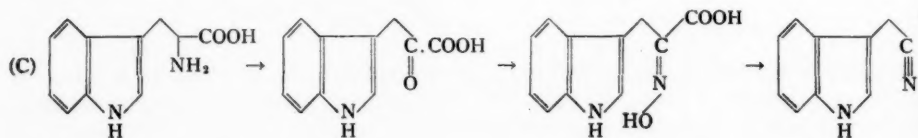
α -imino acids undergo rapid spontaneous hydrolysis to α -keto acids (8) rather than decarboxylation. The latter reaction is feasible, however, since *in vitro* primary amines catalyze α -keto acid decarboxylation (e.g. ref. 9) with the intermediate formation of *N*-substituted α -imino acids (Schiff's bases), which themselves readily decarboxylate (e.g. ref. 9). Such a mechanism, however, is no longer accepted for the enzymatic decarboxylation of α -keto acids (10).

Indirect evidence supporting the first step of sequence B, conversion of tryptophan to indolyl-3-pyruvic acid by transamination, has been accumulating (e.g. ref. 11). The only intermediate in sequence B which has not yet been found to occur is indolyl-3-acetaldoxime. Other oximes, and particularly α -keto acid oximes, have, however, been isolated from natural sources (e.g. ref. 12) and the formation of indolyl-3-acetaldoxime from indolyl-3-acetaldehyde and hydroxylamine is a tenable supposition, since indirect evidence for the occurrence of both these substances in plants is available (6 and 13 respectively). The fact that IAN biosynthesis from tryptophan is inhibited by dimedone, which is regarded as a specific aldehyde trapping agent, has been adduced as an important argument in favor of the implication of indolyl-3-acetaldehyde in the biogenetic sequence (14). The final step of sequence B, although easily accomplished chemically under vigorous, usually anhydrous, reaction conditions, is again without known biochemical analogy.

Neither sequence, however, accounts for the detection by Housley and Bentley (4, 15) of an acidic precursor of IAN in the water-soluble, ether-insoluble fraction of an extract of cabbage leaves. This precursor gave IAN when heated in aqueous solution pH 5.6 at 98–100° for 25 minutes. The same chemical reaction took place to some extent even at room temperature under basic, but particularly under acidic, conditions. Other data (16) also point to the occurrence of a water-soluble, ether-insoluble acidic precursor of IAN.

It should be noted that Housley and Bentley (15) do not present direct evidence bearing on the conversion of their precursor to the nitrile *in vivo*, but infer biological conversion on the basis of the precursor's growth-promoting properties and by analogy with its chemical behavior. Accepting this inference as a working hypothesis, it follows that any substance postulated as direct biological precursor of the nitrile should also be convertible to nitrile under mild chemical conditions. The identity of the precursor with either indolyl-3-acetaldehyde imine (sequence A) or indolyl-3-acetaldoxime (sequence B) must therefore be ruled out.

We have examined the chemical and chromatographic properties of synthetic indolyl-3-pyruvic acid oxime and have found them to be very similar to those of the IAN precursor described by Housley and Bentley. We wish to advance a new hypothesis for the biosynthesis of IAN (sequence C) with indolyl-3-pyruvic acid oxime as the key intermediate:



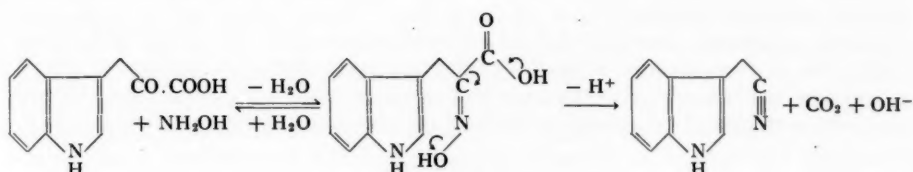
The first step in our sequence is identical with that of sequence B. The second step, *in vivo* conversion of α -keto acid to the corresponding oxime, is not a novel idea (13). Although indolyl-3-pyruvic acid oxime has not been isolated from natural sources, other

α -oximino acids have been obtained from plants (17) and from micro-organisms (e.g. ref. 12) and it has been shown that compounds of this type may be utilized biologically (18, 19), whereas oximes of carbonyl compounds other than α -keto acids are relatively inactive (18, 20). A transoximase system, catalyzing the transfer of $=N-OH$ between α -keto acids, has been detected in a variety of tissues (21). α -Keto acid oximes are thus known as biochemical intermediates.

The novel feature of our sequence lies in the postulated concerted conversion of indolyl-3-pyruvic acid oxime to IAN. We have found that this reaction takes place readily in aqueous solutions pH 1 to 7 at moderate temperatures, as required for an IAN precursor by the results of Housley and Bentley.

Not only indolyl-3-pyruvic acid oxime, but all other α -keto acid oximes we have tested, yield the lower nitrile and CO_2 under these reaction conditions. The generality of this phenomenon was first recorded by Bouveault and Locquin (22) but has since been almost entirely overlooked, except in isolated instances (23). Considering the ease with which the conversion takes place it is not surprising that reaction of α -keto acids with hydroxylamine under the usual conditions gives oxime in poor yield only and that occasionally (e.g., indolyl-3-glyoxylic acid (24)) no oxime, but only nitrile is obtained. It is probable that Bauguess and Berg (25) obtained a very impure sample of indolyl-3-pyruvic acid oxime (m.p. indefinite, $>175^\circ$) by this method. The compound (m.p. 154° (decomp.)) was obtained in 59% yield (26) by nitrosation of ethyl α -acetyl- β -(3-indolyl)-propionate.

When heated in 0.05 M H_2SO_4 for 3 hours, indolyl-3-pyruvic acid oxime is converted to IAN in 95% yield. The same product (60% yield) is obtained directly when equimolar amounts of indolyl-3-pyruvic acid and hydroxylamine hydrochloride are refluxed in aqueous solution, pH 1.

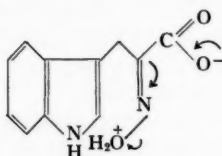


In further confirmation of the ease with which IAN formation takes place, decomposition of oxime to nitrile was found to occur readily even at low temperature. Table I

TABLE I
Yield of IAN on incubation at 41.5° for 24 hours of 20 mg indolyl-3-pyruvic acid oxime in buffer solutions, pH 1-7

Buffer	Initial pH	Final pH	IAN obtained	
			mg	% yield
HCl/KCl	1.0	1.0	6.44	45.0
HCl/KCl	1.6	1.6	7.36	51.4
HCl/KCl	2.0	2.0	7.51	52.5
Phthalic acid/hydrogen phthalate	3.1	3.0	6.73	47.0
Hydrogen phthalate/phthalate	4.0	3.6	5.41	37.8
Hydrogen phthalate/phthalate	5.0	4.5	1.85	12.9
$H_2PO_4^-/HPO_4^{2-}$	7.0	6.3	0.78	5.5

shows the yields of nitrile at various pH values, when a dilute solution of oxime was incubated at 41.5° for 24 hours. The yield of product was optimal at pH 2, decreased at lower pH values, and dropped with rise in pH, but even at pH 7 nitrile was obtained. Although the decreased yields at pH <2 may be due entirely to side reactions leading to destruction of the indole nucleus, this is not likely in view of the good yield of IAN at pH 1 at 100° but may be a consequence of the existence at pH 2 of maximal amounts of the zwitterionic species, which would be the most favorable for a concerted elimination



of carbonic anhydride and water from the oxime. At pH <2 the carboxylate group (pK_a 3.4) would be more than 96% protonated, whereas at pH >2 the oxime OH is unlikely to bear a proton.

A concerted elimination of this type requires an anti (HO- -COOH) stereochemistry of the oxime. Only in very few instances (phenylglyoxylic acid (27), oxaloacetic acid (28), and possibly phenylpyruvic acid (29), glyoxylic acid (30), and α -ketoglutaric acid (19)) have syn- and anti-isomers of α -keto acid oximes been described. The stereochemistry of these oximes has not been reinvestigated by modern methods, and therefore remains uncertain, but on the basis of their classical investigations both Hantzsch (27, 28) and Meisenheimer (31) concur that, where only one isomer is known, the favored stereochemical arrangement of α -keto acid oximes is anti (HO- -COOH), as now required to account for the facility of their conversion to nitriles in aqueous solution by a concerted acid catalyzed mechanism.

Having established that indolyl-3-pyruvic acid oxime yields IAN under mild chemical conditions, as demanded for a precursor according to Housley and Bentley, it remained to compare the behavior on extraction and chromatography of Housley and Bentley's precursor with that of the oxime. In Table II the chromatographic behavior of indolyl-3-

TABLE II

	Precursor	Oxime	IAN
(1) R_f ranges			
2-PrOH/0.15 M NH_3 (4:1)	0.39-0.48	0.40-0.45	0.85-0.90
1-BuOH, saturated with 1.5 M NH_3	0.10-0.15	0.13-0.21	0.85-0.90
(2) Chromogenic sprays			
$FeCl_3/HClO_4$	Yellow	Mauve changing to greenish yellow	Violet blue changing to brown
HNO_3/HNO_2	Yellow	Yellow	Blue-purple changing to greenish yellow
<i>p</i> -Dimethylaminobenzaldehyde		Mauve changing to greenish yellow	Mauve changing to brown
(3) Fluorescence	Bluish-purple	Blue	Blue

pyruvic acid oxime is compared with that of Housley and Bentley's IAN precursor. The similarity of the R_f ranges of the two substances in the solvent systems used by Housley and Bentley is evident. Differences in color with Ehrlich's reagent and $FeCl_3$ /perchlorate

may be accounted for by concentration effects. At low concentrations the mauve color given by indolyl-3-pyruvic acid oxime with these two reagents was exceedingly transient.

Complete analogy was found in the behavior of synthetic oxime and IAN precursor on partition between solvents: using a solution of indolyl-3-pyruvic acid oxime (20 mg in 15 ml 95% ethanol, adjusted to pH 3.2 with dilute sulphuric acid) we duplicated the operations performed by Housley and Bentley in their treatment of those fractions of cabbage extract which contained IAN precursor. The details of this comparison are set out in the experimental section. Housley and Bentley fractionated cabbage extract into ether-soluble neutral, ether-soluble acidic, and water-soluble fractions by extraction with ether after pH adjustment. Their IAN precursor was found, by chromatography and bio-assay, mainly in the water-soluble, but also in the acidic ether-soluble, fraction. Elution of the IAN precursor from chromatograms and rechromatography led to a decrease in IAN precursor and an appearance of indolyl-3-acetonitrile. When we applied Housley and Bentley's procedures to indolyl-3-pyruvic acid oxime, results analogous in all particulars were obtained. In a number of their chromatograms Housley and Bentley detected two other growth active substances (R_f 0.10–0.20 and R_f 0.55–0.65, respectively, in 2-PrOH/ NH_3). Chromatography of the ether extract of an acidified 5% NaHCO_3 solution of indolyl-3-pyruvic acid oxime gave, in addition to the expected spots of starting material and IAN, two weakly Ehrlich-positive spots of unknown nature with R_f ranges, 0.11–0.18 and 0.60–0.70, similar to those of Housley and Bentley. These growth active zones may thus have been due to artifacts derived from their acidic IAN precursor during extraction and chromatography.

The inhibition of IAN formation by dimedone, which has already been referred to, requires explanation. Since under mild conditions dimedone reacts specifically with aldehydes (e.g. ref. 32) it would appear that an aldehyde is implicated in IAN formation. This consideration led Gordon (14) to reject indolyl-3-pyruvic acid oxime as a possible intermediate in IAN biosynthesis in favor of indolyl-3-acetaldehyde. Preliminary experiments have now shown that Gordon's inference was based on insufficient evidence: whereas incubation of indolyl-3-pyruvic acid oxime at pH 2.0 and at pH 5.0, yielded IAN in 52.5% and 12.9% yield respectively (Table I), incubation of the oxime under similar conditions in the presence of dimedone did not yield detectable amounts of nitrile. Instead, the neutral ether-soluble fraction contained an oily yellow material of unknown structure which had no trace of $-\text{CN}$ absorption at 2250 cm^{-1} , and showed, in addition to the indole bands at $280\text{--}288\text{ m}\mu$, an absorption band at $410\text{ m}\mu$, which disappeared in alkaline solution. Incubation of indolyl-3-pyruvic acid with dimedone, either in the presence or absence of hydroxylamine, gave rise to a similar yellow substance. When indolyl-3-acetonitrile was incubated with dimedone, starting material was recovered in 95% yield. Although the nature of the yellow dimedone adducts of indolyl-3-pyruvic acid and its oxime is as yet undetermined, it is clear that dimedone inhibits their conversion to indolyl-3-acetonitrile. This is consistent with Gordon's experimental results (14) on the inhibition of IAN formation from tryptophan in the presence of dimedone in *Avena* coleoptiles.

The auxin activity of indolyl-3-pyruvic acid oxime was compared with that of IAN and of indolyl-3-acetic acid in the *Avena* section (straight growth) test.² The oxime was found to have from 25% to 20% of the auxin activity of indolyl-3-acetic acid (compared

²We are greatly indebted to Drs. J. Shen and S. A. Gordon, Argonne National Laboratory, Lemont, Illinois, for this study.

on a molar basis) over a concentration range of 10^{-4} to 10^{-2} gram moles per liter (Fig. 1).

The chemical reactivity of indolyl-3-pyruvic acid oxime, the behavior of this substance on chromatography and solvent partition, and its biological activity thus correspond to the properties of the IAN precursor described by Housley and Bentley.

The evidence is compatible with the hypothesis that indolyl-3-pyruvic acid oxime is the biochemical precursor of indolyl-3-acetonitrile.

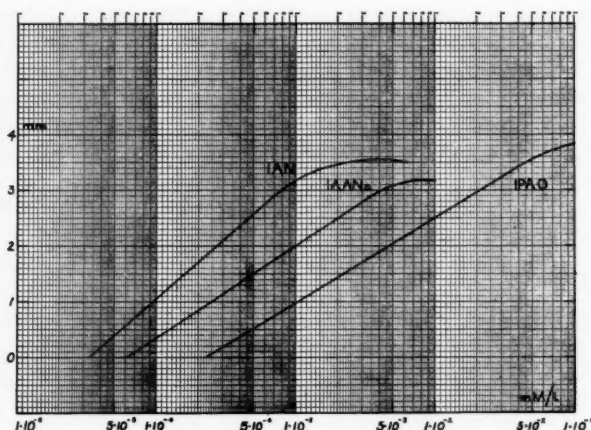


FIG. 1. Auxin activities of indolyl-3-acetonitrile (IAN), sodium indolyl-3-acetate (IAA.Na), and indolyl-3-pyruvic acid oxime (IPA.O) in the *Avena* section (straight growth) test: 3-mm sections; medium: 0.01 *M* NaHCO_3 , containing 2% w/v sucrose (2 ml); 20 hours.

Ordinate: mm increase over original length, corrected for control sections in medium alone (linear scale). Abscissa: concentration of auxin in millimoles per liter (log scale).

EXPERIMENTAL

Indolyl-3-pyruvic acid was prepared according to Bentley *et al.* (5). Indolyl-3-pyruvic acid oxime was obtained from indolyl-3-pyruvic acid (25) and also by nitrosation of ethyl α -acetyl- β -(3-indolyl)-propionate (26), melting at 157° , pK' 3.4 (i.e., pH at half equivalence in saturated aqueous solution), infrared absorption (Nujol) (cm^{-1}): 3360(s), 1690(s), 1620(m); ultraviolet absorption (λ_{max} , $m\mu$ (log ϵ)): 225(4.13), 274(3.83), 282(3.84), 290(3.77).

Indolyl-3-acetonitrile

(1) From Indolyl-3-pyruvic Acid

Indolyl-3-pyruvic acid (0.400 g, 0.00197 mole) and hydroxylamine hydrochloride (0.136 g, 0.00197 mole) in 30 ml water were refluxed 2.5 hours. The solution, which contained a small amount of dark brown precipitate, was filtered, allowed to cool, and extracted with ether (5 times 10 ml). The ether extract was washed with 5% sodium bicarbonate solution and with water, dried over Na_2SO_4 , and concentrated, yielding indolyl-3-acetonitrile as an oily residue. The product was distilled at 100° and 10^{-3} mm and was obtained as a yellow oil (0.184 g, 60%), whose infrared (in CHCl_3) (cm^{-1}): 3450(s), 2250(s), 1615(m), 1455(s), 1350(s), 1330(s)) and ultraviolet (λ_{max} , $m\mu$ (log ϵ)) in MeOH: 220(4.50), 273(3.78), 279(3.80), 288(3.68)) absorption was identical with that of an authentic specimen melting at $35\text{--}36^\circ$, prepared from gramine methiodide (33). The oil crystallized on seeding with a few crystals of the authentic sample.

A small portion of the oily product was converted to the picrate, melting at 127–128° (33).

(2) *From Indolyl-3-pyruvic Acid Oxime*

(i) *At 100°*.—The oxime (0.100 g, 0.00046 mole) was dissolved in 20 ml 0.05 *M* H₂SO₄ (0.001 mole) and the solution refluxed 3 hours in an atmosphere of nitrogen. On cooling, a small amount of dark sediment was filtered off, the solution was extracted with ether, the ether extract washed with 5% bicarbonate solution and with water, dried over Na₂SO₄ and concentrated, and the oily residue distilled at 100° and 10⁻³ mm to yield 0.068 g (95%) indolyl-3-acetonitrile as a light yellow oil, crystallizing on seeding with an authentic specimen.

(ii) *At 40°*.—A solution of oxime (0.020 g, 0.000092 mole) in 20 ml buffer solution was allowed to stand 12 hours at room temperature and then 24 hours at 41.5°. Buffers used were those of Clark and Lubs, HCl/KCl (pH 1, 1.6, and 2), phthalate (pH 3, 4, and 5), and H₂PO₄⁻/HPO₄⁻ (pH 7). Some discoloration was observed at pH 1–4. The solution was extracted with ether; the extract washed with 5% bicarbonate and water, dried over Na₂SO₄ and concentrated; the residue was dissolved in CHCl₃ and identified as indolyl-3-acetonitrile by its infrared absorption. The yield was determined by measuring the intensity of the ultraviolet absorption at 288 mμ of the product in methanol at suitable dilution. Results are summarized in Table I. Incubation of the oxime in the presence of dimedone (0.200 g) was carried out similarly and the reaction mixture was worked up for neutral products in the same way, except that dilute NaOH, instead of NaHCO₃ solution, was used for washing, to remove unreacted dimedone.

Solvent Fractionation and Chromatography of Indolyl-3-pyruvic Acid Oxime

Chromatography.—Solvents used in ascending paper chromatography on Whatman No. 1 paper were (a) 2-propanol/0.15 *M* ammonia (1:4), and (b) 1-butanol, saturated with 1.5 *M* ammonia. Chromogenic reagents applied were (i) Salkowski reagent: ferric chloride/perchloric acid (100 ml 5% aqueous HClO₄ and 2 ml 0.05 *M* FeCl₃); (ii) nitrous acid/nitric acid (1 g KNO₂ in 200 ml HNO₃, sp. gr. 1.42, diluted 10 times); (iii) Ehrlich's reagent (2 g *p*-dimethylaminobenzaldehyde in a mixture of 80 ml absolute ethanol and 20 ml HCl, sp. gr. 1.18) (15).

Solvent fractionation of the oxime according to the procedure used by Housley and Bentley (15) for the investigation of cabbage extract.—For purposes of comparison Housley and Bentley's operations and results at each stage are quoted in square brackets.

Preliminary Fractionation

(A) Indolyl-3-pyruvic acid oxime (20 mg) in 15 ml 95% ethanol adjusted to pH 3.2 with 0.05 *M* H₂SO₄, was stirred at -10° for 40 hours (fraction 1). Chromatography in 2-PrOH/NH₃, *R_f* 0.42, i.e., unchanged oxime. [Frozen ground cabbage was extracted for 40 hours at -10° with 95% ethanol acidified to pH 3.2 with H₂SO₄. Not chromatographed.]

(B) The pH of the solution was adjusted to pH 5 by addition of saturated aqueous Ba(OH)₂, BaSO₄ was filtered off and ethanol removed from the filtrate *in vacuo* at 30° (fraction 2). Chromatography in 2-PrOH/NH₃ gave a spot at *R_f* 0.42, i.e., unchanged oxime. The residual solution was mixed with 3 ml phthalate buffer, pH 3, and allowed to stand at room temperature 24 hours. [Ba(OH)₂ solution was added adjusting the pH to pH 5, the extract was filtered, ethanol removed at 35° *in vacuo* and the pH of the residual solution adjusted to pH 3 with dilute H₂SO₄. Not chromatographed.]

(C) The solution was exhaustively extracted with ether, yielding ether extract (fraction 3) and aqueous layer (fraction 4). Chromatography of the ether layer in 2-PrOH/NH₃

gave spots R_f 0.42 (oxime) and R_f 0.90 (nitrile). The aqueous layer showed a spot at R_f 0.42 (oxime) only. [The solution was extracted with ether, yielding an ether-soluble fraction and a water-soluble fraction.]

The above experiments show that indolyl-3-pyruvic acid oxime is stable at pH 3.2–5 at -10° , but that it is partially converted to the nitrile at pH 3 and room temperature. They also show that the oxime is soluble both in ether and in water. Later steps were carried out with freshly prepared oxime in the requisite solvent.

Investigation of the "Ether-soluble" Fraction

(D) Indolyl-3-pyruvic acid oxime (10 mg) was dissolved in 5 ml ether giving a solution corresponding to fraction 3. This was extracted with 5% NaHCO_3 solution, yielding an ethereal and an aqueous layer. The ethereal layer was dried (fraction 6).

The aqueous bicarbonate layer was acidified to pH 3 with 0.05 M H_2SO_4 . This solution was divided into two portions, one of which was extracted with ether immediately, and the ether layer washed and dried (fraction 5a), the other extracted with ether after 16 hours and the ether layer treated similarly (fraction 5b).

Chromatography of the "neutral" fraction 6 in 2-PrOH/ NH_3 showed a single weak spot of R_f 0.90, i.e., indole-3-acetonitrile. The "acidic" fraction 5b showed an intense spot at R_f 0.90 (indole-3-acetonitrile), and a weak spot at R_f 0.41 (oxime). Fraction 5a showed a strong spot at R_f 0.90 (nitrile), a strong spot at R_f 0.42 (oxime), and in addition weakly Ehrlich-positive spots at R_f 0.60–0.70 (green, changing to yellow, changing to green), R_f 0.42–0.55 (purple, changing to green), and R_f 0.11–0.18 (blue green).

Evidently prolonged exposure to pH 3 had caused almost complete conversion of oxime to nitrile (fraction 5b), whereas during shorter contact with an acid medium (fraction 5a) conversion of oxime to nitrile was incomplete. The nature of the materials giving rise to the additional indolic spots in this fraction is obscure, but it is suggestive that Housley and Bentley report the occurrence, in a number of their chromatograms, of growth active materials of R_f 0.1–0.2 and 0.5–0.7 which could not be ascribed to recognized auxins. It is possible that these materials may have been breakdown products of their precursor, similar to the oxime breakdown products of fraction 5a. [The ether-soluble fraction from step C was washed, dried, concentrated, redissolved in ether, and extracted with bicarbonate solution. The ether layer gave a neutral fraction, containing growth active zones at R_f 0.46–0.90 (mainly IAN, but presumably some precursor, due to incomplete fractionation), whereas the bicarbonate layer, after acidification to pH 3, extraction into ether, and drying and evaporation of the ether layer, showed weak auxin activity at R_f 0.25–0.50 (precursor) and strong activity at R_f 0.54–0.89 (IAN).]

Investigation of the "Water-soluble" Fraction

(E) Indolyl-3-pyruvic acid oxime (10 mg) was dissolved in 5 ml water, giving a solution corresponding to fraction 4 (step C). Chromatography in 2-PrOH/ NH_3 gave R_f 0.42 only. The area of the paper corresponding to the oxime was eluted with 4 ml water, and the eluate concentrated and rechromatographed with 2-PrOH/ NH_3 and also with 1-BuOH/ NH_3 . The former chromatogram showed spots at R_f 0.42 (oxime) and R_f 0.90 (nitrile), the latter at R_f 0.16 (oxime) and R_f 0.90 (nitrile). During elution and rechromatography oxime had thus partially decomposed to nitrile. [The pH of the water-soluble fraction from step (C) was adjusted to pH 5.3 and the solution concentrated at 25° . Chromatography in 2-PrOH/ NH_3 of the concentrate gave a precursor spot at R_f 0.4–0.5 and an IAN spot at R_f 0.8–0.9, the latter presumably due to previous acid treatment. The area on the chromatogram corresponding to precursor was eluted with 4 ml water at 5° and

the eluate rechromatographed with 2-PrOH/NH₃, where it showed *R_f* 0.4–0.5, and with *n*-BuOH/NH₃, where it gave *R_f* 0–0.15. In both the latter chromatograms an IAN spot at *R_f* 0.8–0.9 also appeared. Thus during elution and rechromatography precursor had partially decomposed to IAN.]

(F) Indolyl-3-pyruvic acid oxime (10 mg) was dissolved in 3 ml water and heated under reflux 25 minutes. On cooling, the solution was extracted with ether. Chromatography of the ether extract in 2-PrOH/NH₃ gave spots at *R_f* 0.42 (oxime) and *R_f* 0.90 (nitrile). Chromatography of the aqueous layer gave a weak spot, *R_f* 0.42 (oxime). [The pH of the water-soluble fraction from step C was adjusted to pH 5.3, the solution was concentrated at 25° and heated at 98–100° for 25 minutes, cooled, dissolved in 20 ml aqueous NaHCO₃, and the solution extracted with ether. Chromatography of the ethereal "neutral" fraction showed a weak auxin zone at *R_f* 0.29–0.44 (precursor which according to Housley and Bentley had entered this fraction due to incomplete separation) and a strong zone at *R_f* 0.7–0.95 (nitrile). Elution and rechromatography in 2-PrOH/NH₃ of the zone *R_f* 0.29–0.44 gave rise to more IAN. The aqueous phase was acidified to pH 3 and extracted with ether, yielding an "acidic" fraction, which on chromatography showed auxin activity at *R_f* 0.25–1.00 with activity peaks at *R_f* 0.85–0.92 (IAN, presumably derived from precursor due to acidification during fractionation) and at *R_f* 0.35–0.48 (presumably precursor, but ascribed by Housley and Bentley to indolyl-3-acetic acid, since this region gave a pink color with Salkowski's reagent).]

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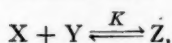
NOTES

A PROPOSED CRYOSCOPIC METHOD FOR DETERMINING THE HEAT OF COMPLEX FORMATION FOR A REACTION, $X + Y \rightleftharpoons Z$

P. A. D. DE MAINE*

Spectrophotometric methods (1, 2, 3) have been used frequently to determine equilibrium constant (K) and heat of formation (ΔH) values for complexes between dissimilar molecules in inert solvents. Scott (4) has reported that such values for K are not reliable; but he (4) and others (5, 6, 7) have noted that ΔH can be determined accurately with spectrophotometric data. Some workers (8, 9, 10) have suggested that the changes in absorption spectra used to determine ΔH (5, 6, 7, 4) arise from changes in the electrical properties of the solution and/or non-specific interactions between the unlike molecules. However, evidence that the changes in spectra are due to specific interactions between the molecules has been reported (11, 12, 13). Thus a non-spectrophotometric method for the determination of ΔH should prove helpful in elucidating the actual nature of the interactions.

If two unlike molecules, X and Y , interact thus,



then

$$[1] \quad K = N_Z / (N_X - N_Z) (N_Y - N_Z)$$

where N_Z , $(N_X - N_Z)$, and $(N_Y - N_Z)$ are the equilibrium concentrations in mole fraction units of Z , X , and Y respectively.

If K_t is the cryoscopic constant (degrees C/mole 100 grams of solvent) of the solvent, then for dilute solutions

$$[2] \quad C_X + C_Y - C_Z = K_a(C_X + C_Y)/K_t,$$

where K_a is the apparent constant calculated for the mixed solute solution with the assumption that $C_Z = 0$.

$$[3] \quad C_X = N_X 100/M, \quad C_Y = N_Y 100/M, \quad C_Z = N_Z 100/M,$$

where M is the molecular weight of the pure solvent.

As N_X and N_Y are known, K and N_Z can be calculated for each mixed solute solution at its freezing point. With the van't Hoff equation (ΔH assumed to be independent of temperature) it can be shown that

$$[4] \quad \Delta T_2 = \frac{\Delta H(\Delta T_1 - \Delta T_2)}{R(T_f - \Delta T_1) \ln (K_1/K_2)} + T_f.$$

K_1 and K_2 are values for the equilibrium constant, in mole fraction units, calculated for mixed solute solutions with freezing points of ΔT_1 and ΔT_2 °C, respectively, below the absolute freezing point (T_f °K) of the pure solvent.

*Present address: Chemistry Department, University of Mississippi, Oxford, Mississippi.

Plots of ΔT_2 versus $(\Delta T_1 - \Delta T_2)/\ln(K_1/K_2)$ for data with ΔT_1 constant should be linear with

$$[5] \quad \text{slope} = \Delta H/R (T_f - \Delta T_1),$$

$$[6] \quad T_f = \Delta T_2 \text{ intercept.}$$

Thus the absolute freezing point of the pure solvent (T_f , °K) and ΔH can be determined with data obtained from measurements with a differential thermometer.

In deriving equations [4], [5], and [6] it has been assumed that (a) activities equal concentration; (b) ΔH is independent of temperature; and (c) both solutes have the same cryoscopic constant.

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CHEMISTRY DEPARTMENT,
NEW YORK STATE UNIVERSITY COLLEGE OF EDUCATION,
135 WESTERN AVENUE, ALBANY 3, N.Y., U.S.A.

CRYSTALLINE O-METHYL ETHERS OF D-GALACTITOL*

C. T. BISHOP

During the course of some work on the separation of carbohydrate derivatives by gas-liquid partition chromatography it was found that anomeric methyl glycosides of methylated monosaccharides were separable (1). The ultimate objective of this work was application of gas-liquid partition chromatography to the structural investigation of polysaccharides; it appeared that the complex mixture of anomers that might be expected from methanolysis of a methylated polysaccharide could be avoided by reduction of the *O*-methyl monosaccharides to the sugar alcohols, which could then be separated as their acetates. It was later found that methanolysis of methylated polysaccharides did not yield as complex mixtures as had been anticipated so this approach was dropped. However, a number of partially methylated sugar alcohols were prepared for use as standard compounds; some of these are readily crystallized, sharp melting, and eminently suitable as characteristic derivatives of the parent monosaccharide. The opportunity is therefore taken to record the preparation and physical properties of 2,4-di-*O*-methyl-; 2,3,4-tri-*O*-methyl-; and 2,3,4,6-tetra-*O*-methyl-D-galactitol; these are derived from

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three *O*-methyl ethers of D-galactose which are found frequently as hydrolysis products of methylated polysaccharides (2).

EXPERIMENTAL

Reductions

The *O*-methyl-D-galactose (100 mg) was dissolved in methanol (3 ml) and potassium borohydride (15–16 mg) was added. The solution was kept at room temperature for 24 hours and then Amberlite IR-120 ion exchange resin was added with shaking until gas evolution ceased. The resin was filtered, washed with methanol, and filtrate plus washings were evaporated to dryness. Addition and evaporation of methanol were repeated six times to remove boric acid. The residues crystallized spontaneously when dried *in vacuo* over anhydrous calcium chloride. Yields were quantitative throughout.

2,4-Di-*O*-methyl-D-galactitol

This compound was prepared by reduction of 2,4-di-*O*-methyl-D-galactose, m.p. 103–104° C, $[\alpha]_D^{25} = +88^\circ \pm 1^\circ$ equilibrium value (*c*, 1.1% in water) (3). The crystalline reduction product was recrystallized from ethyl acetate to a constant melting point of 134–135° C (corr.), $[\alpha]_D^{25} = +23.5^\circ \pm 0.5^\circ$ (*c*, 2.04% in methanol). Anal. Calc. for $C_8H_{18}O_6$: C, 45.70%; H, 8.63%; OCH_3 , 29.64%. Found: C, 45.59%; H, 8.31%; OCH_3 , 29.80%.

2,3,4-Tri-*O*-methyl-D-galactitol

This compound was prepared by reduction of sirupy 2,3,4-tri-*O*-methyl-D-galactose, $[\alpha]_D^{25} = +110^\circ \pm 2^\circ$ (*c*, 1% in water), which had been characterized as its anilide (4, 5), m.p. 166–168° C, $[\alpha]_D^{25} = +42^\circ \pm 3^\circ$, equilibrium (*c*, 1% in methanol) and by conversion to 2,3,4-tri-*O*-methyl-D-galactonamide (5), m.p. 166–167° C, $[\alpha]_D^{25} = +35^\circ \pm 3^\circ$ (*c*, 0.8% in water). The crystalline reduction product was recrystallized from ethyl acetate to a constant melting point of 121–122° C, $[\alpha]_D^{25} = \pm 0^\circ$ (*c*, 1.56% in methanol). Anal. Calc. for $C_9H_{20}O_6$: C, 48.20%; H, 8.93%; OCH_3 , 41.50%. Found: C, 48.07%; H, 8.85%; OCH_3 , 41.85%.

2,3,4,6-Tetra-*O*-methyl-D-galactitol

This compound was prepared by reduction of sirupy 2,3,4,6-tetra-*O*-methyl-D-galactose, $[\alpha]_D^{25} = +109^\circ \pm 2^\circ$ (*c*, 1% in water), which had been characterized as its anilide (6), m.p. 196.5–198° C, $[\alpha]_D^{25} = -137^\circ \pm 1^\circ$ (*c*, 2% in pyridine). The crystalline reduction product was recrystallized from cyclopentane to a constant melting point of 68–70° C, $[\alpha]_D^{27} = +12.5^\circ \pm 0.5^\circ$ (*c*, 2.25% in ethanol). Anal. Calc. for $C_{10}H_{22}O_6$: C, 50.40%; H, 9.31%; OCH_3 , 52.32%. Found: C, 50.64%; H, 9.34%; OCH_3 , 52.61%.

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DIVISION OF APPLIED BIOLOGY,
NATIONAL RESEARCH COUNCIL,
OTTAWA, ONTARIO.

SPIROHEXANE

DONALD E. MCGREER

In 1953 Slobodin and Blinova (1) reported an attempt to synthesize spirohexane by the treatment with zinc dust of 1,1-bis-(bromomethyl)-cyclobutane prepared from the corresponding diol and phosphorus tribromide. The only product isolated in the dehalogenation reaction was methylenecyclopentane. Rearrangement may have occurred in the dehalogenation step since similar rearrangements have been observed to occur as in the preparation of spiropentane (2). It is also possible that treatment of the diol leads to a rearranged dibromide since rearrangement has been noted in the treatment of cyclobutyl carbinol with phosphorus tribromide (3).

Spirohexane has now been prepared in good yield from 1,1-bis-(iodomethyl)-cyclobutane (I) and zinc in the presence of tetrasodium ethylenediaminetetraacetate to remove the zinc ions as formed in the reaction. This method was recently developed by Applequist *et al.* for the synthesis of spiropentane from pentaerythrityl tetrabromide (2). The 1,1-bis-(iodomethyl)-cyclobutane was prepared by the method of Schubert and Leahy (4) and its structure was checked by N.M.R., which showed two unresolved peaks with an area ratio of 2:3 at 104 and 260 p.p. 10^8 from water due to the $-\text{CH}_2\text{I}$ and cyclobutyl hydrogens, respectively. The spirohexane obtained by treatment of I with zinc dust showed no absorption in the infrared spectrum in the region for multiple bonds and had a N.M.R. spectrum which showed two peaks in an area ratio of 3:2 at 289 and 459 p.p. 10^8 from water due to the cyclobutyl and cyclopropyl hydrogens, respectively (5).

Spirohexane has also recently been prepared by the reaction of methylenecyclobutane and methylene iodide in the presence of a zinc-copper couple (6).

EXPERIMENTAL

An "Aerograph" vapor chromatography unit fitted with a 10-ft Ucon Polar column was used with helium as the carrier gas. The N.M.R. spectra were determined on a 40-Mc/s Varian spectrophotometer with field stabilizer VK 3506, and methylene chloride was used as an external standard.

1,1-Bis-(iodomethyl)-cyclobutane (I)

1,1-Bis-(iodomethyl)-cyclobutane, b.p. 76–78° at 0.3 mm, was prepared in 50% yield by the method of Schubert and Leahy (4). A N.M.R. spectrum (0.5 ml/ml of carbon tetrachloride) showed two peaks at 104 and 260 p.p. 10^8 from water with peak areas in the ratio of 2:3, respectively.

Spirohexane

In a 250-ml three-necked flask fitted with a reflux condenser, stirrer, and dropping funnel was placed 21 g of disodium dihydrogen ethylenediaminetetraacetate, a solution of 7.4 g of sodium hydroxide in 13 ml of water, 40 ml of 95% ethanol, and 0.6 g of sodium iodide. The mixture was heated to reflux and 5.5 g of zinc dust was added followed by 6.3 g of 1,1-bis-(iodomethyl)-cyclobutane which was added dropwise over a half-hour period. The mixture was refluxed an additional hour and distilled through a wire gauze column to give 2.8 g, b.p. 56–79°. Separation of the distillate by vapor chromatography gave 0.94 g (60%) of spirohexane, b.p. 70°, n_D^{25} 1.4245, D_4^{24} 0.855. Found: C, 87.65; H, 12.00%. Calc. for C_6H_{10} : C, 87.73, H, 12.27%.

The infrared spectrum (liquid film) showed no bands in the region from 1500 to 2800 cm^{-1} . The N.M.R. spectrum (neat) showed two peaks at 289 and 459 p.p.m.¹⁰ from water with peak areas in the ratio of 3:2 respectively.

In addition to spirohexane the chromatogram of the crude product showed ethanol and an unidentified component for which the peak area was less than 3% of that for spirohexane.

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DEPARTMENT OF CHEMISTRY,
UNIVERSITY OF BRITISH COLUMBIA,
VANCOUVER 8, B.C.

AMINONITRILES. II. SOME DERIVATIVES OF 2-AMINO-3-CYANOINDENE*

D. L. GARMAISE AND S. GELBLUM

As part of a study on the relation between chemical structure and bacteriostatic activity, a series of 2-arylamino- (and α -alkylamino)-3-cyanoindenes was prepared from the readily accessible 2-amino-3-cyanoindene.

The replacement of the unsubstituted amino group in β -iminonitriles (α -amino- β -cyanoethylenes) by anilino groups is normally accomplished (1, 2) by reacting the iminonitrile with the substituted aniline in acetic acid solution. This procedure was found to give variable results when applied to 2-amino-3-cyanoindene, and, in the case of 3-nitroaniline, 3-nitroacetanilide was isolated as the major product. Better results were obtained by heating the iminonitrile and the amine without solvent in the presence of the amine hydrochloride. The superiority of strong acid catalysis is to be expected in this type of nucleophilic addition to α,β -unsaturated systems (3). 2-(3,4-Dichlorobenzylamino)-3-cyanoindene was obtained in 95% yield by heating the iminonitrile and 3,4-dichlorobenzylamine with 5 mole% 3,4-dichlorobenzylamine hydrochloride. The 3,4-dichloroanilino derivative was prepared by simply fusing the iminonitrile with 3,4-dichloroaniline hydrochloride.

Although the action of concentrated sulphuric acid on 2-amino-3-cyanoindene gives 2-amino-3-carboxyindene in good yield (4), similar treatment of 2-(3,4-dichlorobenzylamino)-3-cyanoindene yielded the corresponding amide, 2-(3,4-dichlorobenzylamino)-indene-3-carboxamide, as the only identifiable product. The same amide was unexpectedly obtained when 2-amino-3-carboxyindene was heated with a mixture of 3,4-dichlorobenzylamine and its hydrochloride.

*Report No. 26.

Hydrogenation of 2-amino-3-carboxyindene with platinum oxide in ethanol at atmospheric pressure proceeded until 4 moles of hydrogen were absorbed. A single isomer of 1-carboxy-2-aminohydrindane, m.p. 171–172° C, was isolated.

2-(3,4-Dichlorobenzylamino)-3-cyanoindene was the only member of the series which showed appreciable bacteriostatic activity. It inhibited the growth of *M. pyogenes* var. *aureus*, *Sarcina lutea*, and *Streptococcus faecalis* at dilutions of 1:320,000, 1:160,000, and 1:40,000, respectively, as determined by the serial dilution tube technique. It was ineffective against Gram-negative organisms.

EXPERIMENTAL*

2-Amino-3-cyanoindene

o-Phenylenediacetonitrile (5) (31.1 g, 0.2 mole) was refluxed with sodium ethoxide (1.0 g, 0.015 mole) in ethanol (130 ml) for 1 hour. The product crystallized on cooling, yield 28.4 g (91%), m.p. 193–194° C (lit. reported m.p. 193° C (4)).

2-(3-Nitroanilino)-3-cyanoindene

A solution of 2-amino-3-cyanoindene (1.56 g, 0.01 mole) and 3-nitroaniline (1.38 g, 0.01 mole) in glacial acetic acid (30 ml) was refluxed for 2 hours. The solution was evaporated to dryness, and the residue was crystallized from dilute acetone to give 3-nitroacetanilide (1.32 g), m.p. 150–151° C, and the product (0.12 g, 4.4%), which melted at 225–226° C, after recrystallization from methanol. Anal. Calc. for $C_{16}H_{10}Cl_2N_2$: C, 63.80; H, 3.35; Cl, 23.54; N, 9.31. Found: C, 63.55; H, 3.35; Cl, 23.52; N, 9.54.

2-(3,4-Dichloroanilino)-3-cyanoindene

2-Amino-3-cyanoindene (1.56 g, 0.01 mole) and 3,4-dichloroaniline hydrochloride (1.98 g, 0.01 mole) were heated at 170–230° C for 25 minutes. Crystallization from ethanol gave the product melting at 200–203° C. Yield 2.27 g (75.5%). The analytical sample, m.p. 203–204° C, was prepared by recrystallization from methanol. Anal. Calc. for $C_{16}H_{10}Cl_2N_2$: C, 63.80; H, 3.35; Cl, 23.54; N, 9.31. Found: C, 63.55; H, 3.35; Cl, 23.52; N, 9.54.

2-(4-Chlorobenzylamino)-3-cyanoindene

A solution of 2-amino-3-cyanoindene (1.56 g, 0.01 mole) and 4-chlorobenzylamine (1.41 g, 0.01 mole) in glacial acetic acid (30 ml) was refluxed for 2 hours. The solution was evaporated to dryness and the residue was crystallized from dilute acetone to give the crude product, m.p. 164–167° C. Yield 1.51 g (54%). Crystallization from methanol raised the melting point to 173–174° C. Anal. Calc. for $C_{17}H_{13}ClN_2$: C, 72.73; H, 4.67; Cl, 12.63; N, 9.98. Found: C, 72.74; H, 5.02; Cl, 12.71; N, 10.15.

2-(3,4-Dichlorobenzylamino)-3-cyanoindene

A mixture of 2-amino-3-cyanoindene (15.6 g, 0.1 mole), 3,4-dichlorobenzylamine (17.4 g, 0.1 mole), and 3,4-dichlorobenzylamine hydrochloride (0.08 g, 0.005 mole) was stirred at 170–200° C for 1 hour. The mixture was cooled and triturated in ethanol (300 ml), giving the product melting at 178–179° C. Yield 30.0 g (95%). The analytical sample melted at 180–181° C after crystallization from dilute acetone. Anal. Calc. for $C_{17}H_{12}Cl_2N_2$: C, 64.77; H, 3.84; Cl, 22.50; N, 8.89. Found: C, 64.86; H, 4.08; Cl, 22.53; N, 8.92.

*All melting points are uncorrected. Microanalyses were performed by Micro-Tech Laboratories, Skokie, Illinois.

2-Amino-3-carboxyindene

2-Amino-3-cyanoindene (2.0 g, 0.013 mole) was stirred in concentrated sulphuric acid (20 ml) for 1 hour, during which the temperature rose from 26° C to 35° C. The solution was poured onto crushed ice, and the resulting suspension was allowed to stand for 2 hours. The precipitate was filtered and extracted with 1 *N* sodium hydroxide solution (50 ml). Acidification of the alkaline extract gave the product melting at 186° C (decomp.). Moore and Thorpe (4) reported a melting point of 171° C. Anal. Calc. for $C_{10}H_9NO_2$: C, 68.55; H, 5.18; N, 8.00. Found: C, 68.38; H, 5.37; N, 8.17.

1-Carboxy-2-aminohydrindane

2-Amino-3-carboxyindene (0.485 g, 0.0028 mole) was hydrogenated at atmospheric pressure in ethanol (50 ml) in the presence of platinum oxide (5 mg). A total of 285 ml hydrogen (0.012 mole) was absorbed in 10 hours. The suspension was filtered and evaporated and the residue was crystallized from ethyl acetate (35 ml), giving the completely saturated product, m.p. 171–172° C. Yield 0.12 g (23.4%). Anal. Calc. for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 65.67; H, 9.51; N, 7.73.

A mixture of incompletely hydrogenated products, m.p. 121–123° C, was isolated from the mother liquors.

2-(3,4-Dichlorobenzylamino)-indene-3-carboxamide

I. 2-(3,4-Dichlorobenzylamino)-3-cyanoindene (4.0 g, 0.013 mole) was stirred in concentrated sulphuric acid (50 ml) for 2 hours. The solution was poured onto crushed ice, and the aqueous suspension was allowed to stand for 2 hours. The crude product was filtered and extracted with 1 *N* sodium hydroxide solution (50 ml). Crystallization of the insoluble fraction from methanol gave the pure amide, m.p. 164–165° C. Yield 0.84 g (20%). Anal. Calc. for $C_{17}H_{13}Cl_2NO_2$: C, 61.30; H, 4.24; Cl, 21.20; N, 8.41. Found: C, 61.20; H, 4.36; Cl, 21.04; N, 8.30.

Acidification of the alkaline extract did not yield any identifiable products.

II. 2-Amino-3-carboxyindene (1.0 g, 0.0057 mole), 3,4-dichlorobenzylamine (1.0 g, 0.0057 mole), and 3,4-dichlorobenzylamine hydrochloride (0.02 g, 0.0001 mole) were heated at 175° C for 20 minutes. The mixture was crystallized from ethanol (10 ml), giving the product melting at 164–165° C. Yield 0.90 g (47%). There was no depression on admixture with the product prepared as in I.

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L. G. RYAN RESEARCH LABORATORIES,
MONSANTO CANADA LIMITED,
LASALLE, QUE.



NOTES TO CONTRIBUTORS

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